University Of Alberta

1977-1999 Canadian Mortality Trends Associated with Motor Neuron Diseases

By

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A thesis submitted to the Faculty of Graduate Studies and Research in partial fulfillment of the requirements for the degree of Master of Nursing

Faculty of Nursing

Edmonton, Alberta

Fall, 2007

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Ottawa ON K1A 0N4
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Your file Votre référence
ISBN: 978-0-494-33179-8
Our file Notre référence
ISBN: 978-0-494-33179-8

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Canada

Dedication

This thesis is dedicated to Wayne Goode who gives me inspiration and whose love, support and friendship carried me through this thesis and strengthens me. Thank-you. We did it together.

Special thanks to my parents Anita and Jim: for their love, support and companionship in this endeavor. To my dad for being a devoted caregiver and for provide care with both compassion and pride. To my mom for her unconditional love and encouragement. Special thanks to my sister and friend Monica, for her ongoing support and love which blesses my life.

This thesis is also dedicated to the orphans of Tanzania, my nieces Katrina, Erika, and my godchild Nicholas.

Completed in memory of Daryl.

Abstract

Motor Neuron Disease (MND) is a group of devastating diseases that cause a profound state of disability leading to an eventual premature death. Five Canadian studies have investigated mortality trends of MND. Of these five studies, the most recent was completed and published nearly a decade ago. As such, there is limited current knowledge regarding how often MND affects Canadians. The purpose of this study was to examine MND mortality trends in Canada, to determine whether MND is becoming more or less common and to explore other socio-demographic trends associated with MND. Descriptive-comparative statistics were used to identify and compare annual MND prevalence and socio-demographic data from a statistics Canada mortality database for the years 1979 through 1999. Seven research questions addressing: (a) prevalence rate, b) age, (c) gender, (d) birthplace, (e) marital status, (f) province of residence, and (g) location of death were used to guide this research study. Five major findings resulted from this thesis study. First, this thesis study established MND are a rare cause of death in Canada with a slight increase in the prevalence rate of MND over the 21-year study period. Second, among the 9,028 people who were recorded as having died of MND, a slight but significant increase in average annual age at death was noted from 1979 through 1999. Third, this thesis study established individuals dying of MND are more often married than not married. Fourth, a slight but significant increase in female cases of MND occurred over time. Lastly, this thesis study established more individuals with MND die in hospital that in other locations. As such, the findings of this study have implications for practice, programs, policy, and research.

Acknowledgements

I would like to acknowledge the time and effort of my Thesis Committee.

First and foremost, I would like to thank Dr. Donna Wilson, my thesis supervisor, for her commitment and guidance in this thesis. I am grateful for her expertise, knowledge and assistance in completing this thesis.

I also would like to thank my committee members Dr. Koop and Dr. Fast for their guidance and interest in this thesis as well as the generous contribution of their time.

I learned a great deal from all of you and greatly appreciate your patience and knowledge.

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CHAPTER ONE

Introduction

Motor neuron diseases (MND) are a group of progressive neurological disorders that destroy the motor neurons that control voluntary muscle activity (Mayeux, 2003). MND includes progressive muscular atrophy, progressive bulbar palsy, primary lateral sclerosis, spinal muscular atrophy, and amyotrophic lateral sclerosis (Swash & Desai, 2000). Brain introduced the concept of "motor neuron disease" in 1962, as this concept recognizes the relationships between these disorders, with all having upper and lower motor neuron involvement, and all having muscle wasting (as cited in Swash & Desai, 2000).

Amyotrophic lateral sclerosis (ALS) is widely considered the most common MND (Gunnarson, Lindberg, Soderfeldt & Axelson, 1991; Mayeux, 2003; Thompson & Swash, 2001). Spinal muscular atrophy and primary lateral sclerosis are variants of ALS (Rowland, & Shneifer, 2001). ALS was first introduced as a disease by the French neurologist Jean-Marin Charcot in 1865 after he noticed an association in the spinal cord between deterioration of the lateral tract and the disappearance of motor neurons in the anterior horn (Le Forestier et al., 2001; Swash, 2001; Thompson & Swash, 2001). ALS is frequently referred to as Lou Gehrig's disease in memory of the famous baseball player who died of ALS in 1941 (Walling, 1999).

The terms ALS and MND have been used interchangeably (Thompson & Swash, 2001), although this thesis will use the term MND - as it has become the more common label for the group of neurological disorders that includes ALS. The

term of MND also avoids the issues arising from ALS having two meanings (Rowland & Shneider, 2001). In the United Kingdom, ALS is used to refer to the large group of disorders listed above, all of which are characterized by progressive degeneration of motor neurons in the central nervous system (Rowland & Shneider). The other definition of ALS, commonly used in the United States and Continental European countries, considers ALS as a specific form of MND (Thompson & Swash). In this definition, "Amyotrophic" is defined as the muscle atrophy, weakness, and fasciculation that signify disease of the lower motor neurons (Rowland & Shneider). "Lateral sclerosis" refers to the hardness of the anterior and lateral columns of the spinal cord that is caused by atrophy of the anterior horn cells and replacement of the large motor neurons by fibrous astrocytes (Walling, 1999).

Anterior Horn Cell disease is yet another term that could be used to refer to MND. Anterior Horn Cell disease comprises another grouping of progressive degenerative disorders of the motor neuron (Krivickas, 2003). These disorders include spinal muscular atrophy, ALS, and ALS variants (Krivickas). MND is thus the more inclusive term.

Research on MND is needed because all MNDs lead to progressive disability, paralysis, and premature death (Majoor-Krakauer, Willems & Hofman, 2003). The initial symptoms of MND include muscle twitching, cramping, and stiffness; as well as muscle weakness affecting an arm or a leg (Mayeux, 2003). As symptoms progressively worsen, muscle atrophy becomes apparent - such as a spastic, complicated gait (Walling, 1999). The afflicted person experiences painful

joint complications from immobility, as immobility is a normal result of muscle weakness and spasticity (Walling). Slurred and nasal speech is generally present, along with difficulty in chewing and swallowing (Mayeux). There is often a lack of spontaneous automatic swallowing to clear saliva in the mouth, with this leading to drooling (Walling). When the cough reflex is weakened by flaccid paralysis of the pharynx, larynx, and respiratory muscles; the aspiration of food and saliva into the airway is all but inevitable (Thompson & Swash, 2001). People suffering from MND typically progress to a profound state of disability and many face decisions about life support, including ventilator assistance and gastrostomy insertion for nutrition purposes (Walling). Regardless, respiratory failure is the most common cause of MND death (Lyall, Donaldson, Polkey, Leigh & Moxham, 2001; Walling, 1999). The following text provides additional more specific information on MND; divided into an overview of implications of the disease progress of MND, the etiology or causes of MND, the significance of MND, and the implications of this thesis study. This chapter concludes by listing the purpose of the thesis investigation and the research questions that guided this study.

Implications of the Disease Progress of MND

There is no cure for ALS or any other MND (Oliver, 2004; Thompson & Swash, 2001). A diagnosis of MND is thus usually devastating for individuals and families. This diagnosis is often delayed, as vague initial symptoms, such as muscle twitching and stiffness, may cause individuals with MND to deny having a health problem and subsequently delay accessing medical care. Eventually, as symptoms progress, individuals with MND experience muscle pain and weakness resulting in

a difficult or complicated gait (Walling, 1999). When medical care is accessed, individuals with MND often undergo extensive testing to establish a diagnosis of MND (Walling). The MND diagnosis is frequently delayed, as there are inadequate diagnostic tools and considerable lack of medical awareness regarding MND (Swash, 2001). Throughout this early stage of MND, the growing physical challenges coupled with an uncertain future often cause enormous emotional stress (Oliver, 2004) Physical distress and many other problems, such as loss of income due to job loss is another feature of the often long process needed to establish a MND diagnosis. When an individual is finally diagnosed with MND, the news that MND is incurable and virtually untreatable is often devastating (Oliver, 2004; Thompson & Swash, 2001).

During the initial phase of obtaining a diagnosis and then over the course of the ensuing illness, the support of friends and family is invaluable. However, as the disease progresses, individuals with MND lose the ability to physically interact with and communicate with their loved ones. Slurred and nasal speech are the first apparent signs of speech problems (Mayeux, 2003). Although the drug Riluzole has been shown to slow deterioration in muscle strength and to increase survival by 3 to 6 months, the treatment of MND typically involves the management of symptoms and is thus primarily palliative in nature (Groenveld et al., 2003; Thompson & Swash, 2001). As MND normally occurs in adulthood, individuals with MND may become deeply depressed and isolated as they lose the ability to communicate, physically interact with, financially provide for, and otherwise care for themselves and their families.

In time, MND progresses to where individuals cannot complete basic activities, such as eating without aspirating food and salvia (Thompson & Swash, 2001). Not only are families and friends affected by this deterioration through their needing to provide an increasing amount of assistance over time, but they too are at risk of becoming depressed and emotionally exhausted (Oliver, 2004). Support systems and MND sufferers often become drained.

Although inventions such as gastrostomy tube feeding and ventilator support provide continued life for individuals with MND, ethical issues arise with these interventions (Oliver, 2004). Prolonged survival in the case of a terminal illness raises questions about whether or not to initiate artificial life supports, particularly for persons who are in a progressively debilitated state that will not be reversed through the use of these life supports (Smyth, Riedl, Kimura, Olick & Siegler, 1997). The central ethical problem, faced by most individuals with MND and their families, is whether to elect to undergo a tracheotomy for long-term mechanical ventilation (Rowland & Shneider, 2001). Although this procedure prolongs life and may thus prolong suffering, it also allows individuals with MND and their families additional time together, including the opportunity for closure. As decisions about life support initiation and their later withdrawal are difficult, additional formal and informal supports during these decision-making processes are required for both the individuals with MND and their families (Young et al., 1994).

Another problem with MND is that the affected individuals may not be able to continue to participate in their health care and other decisions. People with MND may remain cognitively intact throughout most of their illness even though their

bodies are deteriorating (Smyth et al., 1997; Young, Marshall & Anderson, 1994). However, cognitive dysfunction can be an integral component of the disease process (Strong, 2001). For this reason, advance care directives should be discussed with MND victims and their families before neurological deterioration occurs. Although this discussion may be difficult, an advance directive is a supportive measure – since it fosters the dignity of the person dying of MND and removes unnecessary decisions from the family. However, in some cases, advanced directives do not provide sufficient or clear care instructions, making it more difficult for families who are then asked to make life support decisions. Furthermore, some individuals with MND are not accepting of either the natural end to life that would occur without life support or an end to life that has been prolonged through life support. These persons may seek an early termination of their life.

Sue Rodriguez, a Canadian woman diagnosed with ALS, brought attention to this ethical and legal dilemma after she attempted to win the right to physician-assisted suicide (Kluge, 1993). According to Kluge, the progressive and deteriorating nature of ALS violated her sense of dignity, as she would not be able to care for herself. She wanted to avoid this by receiving physician-assisted suicide at a time of her choice. Kluge (1993) argued that the ethical principal of beneficence was violated by the disallowance of physician-assisted suicide because her emotional well-being was harmed as the disease progresses. This illustration of Sue Rodriguez's case demonstrates that a diagnosis of MND requires an individual with MND and their family to face many difficult ethical choices, in addition to

physical and emotional challenges.

MND Etiology

Despite considerable research, the etiology or cause of MND remains unknown (Al-Chalabi & Leigh, 2000; Thompson & Swash, 2001). Several causative theories and risk factors have been suggested, with aging and family history considered the only established risk factors to date (Rowland & Shneider, 2001). It is generally thought that the incidence of MND increases with age, as an ALS diagnosis is rare before the age of 40 (Majoor-Krakauer et al., 2003). Specific genes have also recently been identified and associated with a hereditary or familial form of ALS (Majoor-Krakauer et al.). It is now believed that 5 to 10 percent of all cases of ALS are familial, the remaining are considered "sporadic," as there is no known cause (Rowland & Shneider). Twenty percent of the familial ALS cases are also believed to be due to mutations in the genes encoding superoxide dismutase 1 (SOD1) on chromosome 21 (Rowland & Shneider). Although there are several possible explanations, it is not known how this alteration in SOD1 induces ALS (Strong, 2001). Other gene disorders have also been associated with ALS, including the ALS2 gene on chromosome 2 (Majoor-Krakauer et al.). Furthermore, an ALS4 gene on chromosome 9 was discovered recently (ALS Society, 2006). ALS 4 gene on chromosome 9 is considered responsible for a rare form of familial ALS that affects boys during their teens and women in their thirties (ALS Society).

MND has also been attributed to a number of biological processes as well. A biological hallmark of ALS is the accumulation of neurofilaments in the cell body and motor neuron (Majoor-Krakauer et al., 2003). Neurofilament proteins are

composed of subunits that participate in axon transport, and have a role in determining the shape of cells and the caliber of axons (Rowland & Shneider, 2001). Disorganized neurofilaments may induce toxicity in the SOD1 gene by impeding the axonal transport of molecules (Rowland & Shneider). A related theory is protein aggregation. Accumulations of proteins have been observed in the anterior horn cells of patients with SOD1 gene mutations (Al-Chalabi & Leigh, 2000). It is thought that protein aggregations damage the cell and prevent normal cell function (Stuban, 2004). However, the exact biological process remains unknown (Al-Chalabi & Leigh).

Mitochondria dysfunction also contributes to the development of ALS (Strong, 2001). An early trait of mutated SOD1 gene is mitochondria dysfunction (Al-Chalabi & Leigh, 2000). Mitochondria dysfunction may occur as a result of oxidation damage including oxidation damage to SOD1 gene (Strong). Several other biological theories are emerging regarding the cause of mitochondria dysfunction (Strong, 2001).

Another biological theory, one that does not involve mitochondria dysfunction, involves excitotoxicity (Majoor-Krakauer et al., 2003). Excitotoxicity refers to prolonged activation of excitatory amino acid receptors, which results in motor neuron death (Majoor-Krakauer et al.). This theory has been considered for many other neurodegenerative disorders (Al-Chalabi & Leigh, 2000). In particular, glutamate is an excitatory neurotransmitter in the motor neuron system, with increased levels of glutamate found in the cerebral spinal fluid of persons with ALS (Majoor-Krakauer et al.). It is believed that glutamate contributes to ALS because it

is not eliminated after nerve conduction. It then causes a toxic over-exposure that disrupts cell function and eventually causes cell death (Stuban, 2004). The drug Riluzole, mentioned earlier as a symptom control and life-prolonging measure, is an antiglutamate drug. As such, it has been found to provide some therapeutic effects (Majoor-Krakauer et al.). This drug may not assist all persons with MND, however, as there are several other neurotransmitters that may cause excitotoxicity (Majoor-Krakauer et al.).

Other biological theories for MND include copper toxicity, persistant viral infections, autoimmunity, and many others (Al-Chalabi & Leigh, 2000). Their exact biological mechanisms remain unknown (Al-Chalabi & Leigh). More research is required to further understand the biological or cellular role in the development of MND.

Another theory that has been considered in the pathogenesis of MND is the gene-environment interaction. Gene-environment interaction occurs when a specific environmental risk factor is introduced within a susceptible population, resulting in their increased risk of acquiring ALS (Majoor-Krakauer et al., 2003). This theory may explain the high incidence of ALS in the West Pacific (Steele & Guzman, 1987). Harry Zimmerman, a navy pathologist, first reported an ALS cluster in Guam in 1945 (Steele & Guzman). ALS was identified at that time as 100 times more common than anywhere else in the world (Steele & Guzman). Many years later, a researcher named Spencer reported that cycad seeds, a stable diet for the Chamorros natives in Guam, resulted in the development of ALS (Steele & Guzman). The gene-environment interaction may be further applicable to this

population as neurofilament aggregation, a biological hallmark of ALS, was found among the Chamorros population in Guam (Majoor-Krakauer et al.). The cycad seeds may be more harmful to this population because these people have a genetic predisposition to neurofilament aggregation (Majoor-Krakauer et al.).

Another possible environmental risk factor for ALS is dietary glutamate (Neilson, Matkin, Longstreth & McGuire, 2000). Individuals with a diet high in glutamate have a more than three times higher risk of developing ALS as compared to those with a diet low in glutamate (Neilson, Matkin, Longstreth & McGuire). Exposure to a high level of dietary glutamate, in combination with glutamate excitotoxicity as discussed earlier, could cause cell death among motor neurons (Neilson et al., 2000). Further research is needed to determine the association between dietary glutamate and cellular glutamate excitotoxicity.

Occupational exposure to certain chemicals is also thought to be an environmental risk factor for MND. According to McGuire, Longstreth, Nelson, Koepsell, and Checkoway (1997), various chemicals used in agricultural work have been associated with a twofold increase in risk. As a higher frequency of ALS among agricultural workers has been reported, this suggests environmental toxic agents such as pesticides may be the root cause (Giagheddu et al., 1983; Granieri et al., 1988; Kalfakis, Vassilopoulos, Voumvourakis, Ndjeveleka & Papageorgiou, 1991; Mandrioli, Faglioni, Merelli & Sola, 2003). Occupational exposure is also illustrated by the finding that military personnel have higher rates of ALS than persons who have not served in the military (Weisskopf et al., 2005). However, Weisskopf et al.'s study comparing military rates and non-military rates was

unclear regarding whether this high military rate is due to the exposure to toxic or infectious agents that were specific to the Gulf War, or to some other aspect of military life. Exposure to heavy metals has also been cited as a possible risk factor for ALS (Mandrioli et al.), although this risk factor has not confirmed by any studies to date (Armon, 2001).

Other risk factors include strenuous physical activity (Majoor-Krakauer et al., 2003). According to Longstreth, McGuire, Koepsell, Wang, and van Belle (1998), ALS develops due to exposure to a neurotoxin that is produced during strenuous physical activity (Walling, 1999). A history of trauma to the brain and spinal cord has been considered another risk factor. (Majoor-Krakauer et al.). Cruz, Nelson, McGuire, and Longstreth's (1999) study, however, found no consistent association between ALS and physical trauma.

Cigarette smoking has also been considered a risk factor for developing ALS. According to Kamel, Umbach, Munsat, Shefner, and Sandler (1999), cigarette smoking is associated with a 70% increase in risk. Cigarette smoking is thought to cause oxidation damage contributing to the development of ALS (Kamel et al., 1999).

In summary, although many theories exist, the cause or causes of MND remain largely unknown. What appears to be common among all these theories is that aging is a factor, since MND is uncommon among youths, and that there is a gene through which time or exposure to certain conditions contributes to an increased risk of acquiring a MND (Rowland & Shneider, 2001).

MND Significance

As indicated above, many risk factors and theories have been developed over time to attempt to understand why people develop MND. MND is a relatively rare group of diseases, with rarity serving to complicate this determination of their etiology. However, the progressive nature of MND and the outcomes of its progression show MND is a significant illness causing premature death, and thus one that should be studied.

A number of MND studies have investigated mortality trends. Mortality trend studies normally report upon decedents each year, including information on socio-demographic or other variables. Research on MND mortality trends is necessary to provide information on life expectancy and many other critical components of information relevant to health policy and personal decision-making. For instance, it is generally assumed that persons who die of MND die prematurely (Walling, 1999). Over time, however, health care technology developments and other developments could be having major effects on life expectancy. People with MND may be living longer, but also experiencing longer periods of dependency, with major subsequent implications for formal and informal support needs.

Mortality data is easily available through death certificate databases, as compared to prevalence and incidence data that are more difficult to collect through searching physician billing records or hospital records, or through requesting such information from family practice physicians or specialists. The prevalence rate is defined as the number of individuals with a certain disease in a population at a specified time divided by the number of individuals in that population at that time

(Medical Dictionary, 2006). The incidence rate is defined as the number of new cases of a disease occurring in a population during a defined time interval, which is usually one year (Medical Dictionary). The mortality rate is defined as the number of deaths from disease per 1,000 population, with this typically reported on an annual basis (Medical Dictionary).

A growing number of studies worldwide have been undertaken on MND mortality, incidence, and prevalence rates. Few Canadian studies on MND mortality trends, and even fewer on MND incidence and prevalence, have been undertaken, however. Only five Canadian studies can be identified, with their foci outlined below.

1. Most recently, Mandler et al. (2001) published an ALS research study that included a location-of-death variable. Their sample of 1,014 people diagnosed with ALS comprised both Americans and Canadians. In this study, the researchers examined end-of-life patterns and therapy for persons with ALS who died between July 1997 and August 2001. Unfortunately, Canadians findings were not reported separately from American findings, so an understanding of Canadian cases is gained.

2. Svenson, Cwik, and Martin (1999) published the most recent prevalence rate of MND in Canada. They determined the prevalence rate of MND in Alberta for the one-year period from 1994 to 1995. These researchers also calculated the mean age when diagnosed and the percentage of people who died during the study period.

3. Prior to this, Buchman, Eisen Hoirch, Schecter, and Sheps (1988)

published a study investigating the epidemiology of ALS in British Columbia. This study, which was summarized in a published abstract that was two paragraphs in length, examined the male/female ratio of ALS, mean age of onset of ALS, annual incidence rate, and age-specific incidence rates of ALS.

4. Murray et al. (1987) investigated the incidence of ALS in Nova Scotia from 1974 to 1984. They also investigated the male to female ratio of ALS.

5. Hudson, Davenport, and Hadler (1986) investigated the incidence, prevalence, and mortality rate of ALS in southwestern Ontario from 1978 to 1982. They also investigated age at diagnosis and duration of illness.

Although helpful, these five Canadian studies do not examine the links between gender, mortality, location of death, marital status, province of residence, and country of origin. In short, research on Canadian MND mortality trends, particularly population-level research has not been completed in recent history. Doing so, will provide valuable information for many practical purposes.

Research Purpose

The purpose of this study was to examine MND mortality trends in Canada, to determine whether MND is becoming more or less common, and to explore other socio-demographic trends associated with MND.

Research Questions

The research questions that guided this study are as follows:

1. What was the prevalence rate of MND in Canada, as determined by national mortality data for the years 1979 through 1999?

2. What are the age trends among MND decedents in Canada for the years

1979 through 1999?

3. What are the gender trends of MND decedents in Canada for the years 1979 through 1999?

4. What birthplace trends for those born within Canada or outside Canada are notable among MND decedents for the years 1979 to 1999?

5. What marital trends of MND decedents in Canada are notable for the years 1979 through 1999?

6. What provincial trends in MND decedents can be identified for the years 1979 through 1999?

7. What trends in hospital or non-hospital location of death for MND decedents in Canada can be identified for the years 1979 through 1999?

Implications of Study

As indicated in the introduction, MND is a progressive, debilitating, incurable, and thus chronic condition leading to a premature death. MND is among the most severe and rapidly progressing chronic illnesses. It is therefore important to investigate the changing rates of MND in Canada over time. This research will provide insight into the cause of MND and will determine whether MND is becoming more or less common over time in Canada. This information will be valuable for planning health care and support programs for individuals with MND and their families.

Individuals with MND typically require both informal and formal care. Spouses often play a significant role by become informal caregivers to their ill partner (Burton, Zdaniuk, Schult, Jackson & Hirsch, 2003). Individuals with MND

or any other chronic illness who have a caregiver or caregiver network are fortunate. Anyone who is not married and childless is at particular risk of unmet needs and institutionalization. One study found seniors who are not married, childless, and in poor health to be the least likely to have a strong support network (Keating, Otfinowski, Wengler, Fast & Derksen, 2003). Researching whether individuals with MND are married or not provides insight into whether they have a support system.

However, support and caregiving networks often become drained for individuals with MND who are married or not. Spouses and other informal caregivers may experience emotional strain as they often feel overwhelmed with the never-ending work needed to ensure the afflicted person has their needs addressed (Boeije, Duijnstee & Grypdonck, 2003). The chronically-ill person and their caregivers may also experience financial strain as caregiving and employment are often incompatible (Boeije, Duijnstee, & Grydonck; Chipchase & Lincoln, 2001). Care providers may experience depression, and other emotional strains, which explains why they often rate their own health as poor (Burton, Zdaniuk, Schult, Jackson & Hirsch, 2003). This strain of caregiving for spouses may cause memory loss and increased physical complaints (Chipchase & Lincoln).

Investigating the mean age at death of individuals diagnosed with MND is thus significant with regard to caregivers and caregiving. Individuals with MND are often older at the time of death. Subsequently, if individuals with MND are married, their spouses are likely to be older. A network comprised only of elderly members will become less able to meet the demands of long-term caregiving, as

these caregivers become more frail over time (Fast et al. 2003). By 65 years of age, 77% of men and 85% of women are now thought to have at least one chronic ill health condition (Gilmour & Park, 2003). As such, old age has implications for the capacity for spousal caregiving. The physical burden associated with chronic conditions is especially challenging for seniors (Gilmour & Park). When the ability to complete activities of daily living diminishes, formal and/or informal care is required.

With the emerging focus on home-based care, there is an increasing demand on the spouse and other family caregivers to look after the chronically-ill person at home (Cheung & Hocking, 2004). Thus, researching the location of death for individuals with MND is relevant to caregivers and individuals with MND. If more individuals with MND are dying at home, then considerable informal and formal supports are likely to be required. When spousal and family support is unavailable and formal support is lacking, then individuals with MND can be expected to have more unmet needs and are more likely to die in hospital or in a nursing home.

Formal care may be especially necessary for women suffering from MND. Spouses are most often the persons who become the informal caregivers, shouldering a large portion of care in the home and broader community (Canadian Institute for Health Information, 2000; Carstairs & Beaudoin, 2000). Investigating the gender of individuals with MND will thus provide insight into the care needs of women with MND. If women suffer from MND more often than men, they may have more unmet care needs and subsequently require more formal care. Women with MND and men who do not have a spouse or family may need to move from a

private residence into an institution to have their care needs met.

Gender-based MND research will also establish whether there are any disease-specific differences between males and females. Gender-based differences are common in many diseases, with some diseases more common to one gender or exclusively to that gender. As such, gender-based MND research will provide insight into the detection, prevention, and cause of MND.

In summary, there are many reasons for a Canadian study of MND mortality trends. Information from such a study will inform both informal and formal care provision. This research will also provide insight into the cause, detection, and management of MND. Research on MND mortality trends will also serve to raise attention to this severely debilitating condition, with policy and practice developments possibly ensuing. As such, many benefits from this research are anticipated for individuals with MND, their families, caregivers, health care professionals, and the general public.

CHAPTER TWO

Literature Review

A thorough literature search of nursing, medical, and psychological databases was completed to obtain relevant literature for a comprehensive research-based knowledge background on MND. The databases used to complete this search were CINAHL for the years 1982 to 2006, PsychInfo for the years 1872 to 2006, Embase for the years 1988 to 2006, Medline for the years 1966 to 2006, and HealthStar for the years 1975 to 2006. The search terms were: Motor Neuron Disease (MND), Amyotrophic Lateral Sclerosis (ALS), Anterior Horn Cell disease, Lou Gehrig's disease; combined with the search terms: Morbidity, mortality, incidence, prevalence, clustering, and epidemiology. Research articles on mortality trends and epidemiology considerations associated with MND were retained and examined. This chapter discusses the retained findings of this search, including a comparison of Canadian research and research completed outside of Canada.

Review Findings

Many articles were identified for potential review through this search process. After a review of all abstracts, and in many cases full papers, a total of 142 articles were retained and reviewed, none of which investigated mortality trends or epidemiological considerations associated with Anterior Horn Cell disease. Most research articles focused on ALS, with MND studies less common. All of the retained articles provided research or information relevant to this study. As such, this material provided foundational knowledge for this thesis study, including the determination of differences in findings among and between the international and

Canadian research. In doing so, this review clarified whether Canadian findings are unique or similar to other countries. Also, as it became evident that limited MND research has been completed in Canada, the international research supplements and advances an understanding of MND. The following chapter of literature review findings is divided into sections focusing on: (a) geographical incidence, prevalence, and mortality rates, (b) age, (c) gender, (d) birthplace, (e) marital status, (f) province of residence, and (g) location of death – in keeping with the thesis research questions. The only exception is that the geographical findings that inform thesis research question 1 and the province of residence findings that inform thesis research question 7 are combined. A discussion of the research literature occurs at the end of each section and at the end of this chapter. This discussion highlights comparisons between and among the studies, as well as discrepancies and gaps in the literature.

MND Geographical Findings

This section reviews the international and Canadian research on incidence, prevalence, and mortality rates of MND. The following literature review first involves a description of research findings on the Canadian incidence, prevalence, and mortality rates of MND, followed by corresponding international findings. A discussion of the Canadian and international literature is then provided to reveal geographic variations or similarities in the incidence, prevalence, and mortality rates of MND. A description of the highest and lowest reported incidence, prevalence, and mortality rates of MND follows.

Canadian MND Province of Residence - Incidence, Prevalence, and Mortality Research Findings

Four published studies reported incidence, prevalence, and/or mortality rates of MND for four specific Canadian provinces. None reported pan-Canadian findings. More specifically, incidence, prevalence, and/or mortality MND rates have been researched in the provinces of British Columbia, Nova Scotia, Ontario, and Alberta.

Incidence rates were reported for three provinces. In Ontario, the average annual incidence rate of MND was 1.63 per 100,000 population from 1978 through 1982 (Hudson, Davenport & Hadler, 1986). During a similar period of time, the incidence rate of MND in Nova Scotia was found to be nearly double the rate identified for Ontario, as in 1979-84, the incidence rate of MND in Nova Scotia was 2.40 per 100,000 population (Murray et al., 1987). A lower rate was reported for ALS in British Columbia, as the incidence rate of ALS in British Columbia was 0.99 per 100,000 population for the 1981-84 period (Buchman et al., 1988).

Prevalence rates were reported for Alberta and Ontario. The prevalence rate in 1983 of MND in Ontario was found to be 4.9 per 100,000 population (Hudson et al., 1986). A higher prevalence rate was reported 12 years later in Alberta, as the prevalence rate on July 1, 1995 of MND in Alberta was found to be 6.07 per 100,000 population (Svenson, Cwik & Martin, 1999).

Only one research study investigated the mortality rate of MND in a Canadian province. Hudson, Davenport, and Hadler (1986) reported that the mean mortality rate of ALS in Ontario was 1.52 per 100,000 population.

Discussion of Canadian MND Prevalence, Incidence, and Mortality Research Findings

As indicated above, incidence, prevalence, and/or mortality rates for MND have been researched in only four provinces: Alberta, Ontario, British Columbia, and Nova Scotia. No national studies have been completed. Some differences in incidence and prevalence are apparent between the provinces. These variations may be the result of true differences in incidence and prevalence, although these differences may also be due to the small number of MND cases in each province, or the outcome of different research methods. For instance, Buchman et al.'s (1988) study that was reported in abstract form did not document any details about the study methodology. Methodological issues are also apparent with Murray et al.'s (1987) study. In this study, the researchers reported that information was collected on ALS diagnoses from all clinical neurologists, neurosurgeons, psychiatrists, and neuropathologists in Nova Scotia (Murray et al.). One methodological issue with this data collection method is the accuracy of information provided from each medical office, as these data were not likely to have been routinely gathered. Furthermore, psychiatrists and neuropathologists do not diagnose ALS, and they may not be privy to this information. Collecting information from these professionals on ALS diagnoses could mean inaccurate information was obtained. It is also possible that some persons with ALS are counted more than once, as they could be receiving health care services from more than one medical office. Another issue is that the data for this study were collected 20 years ago, MND rates could be very different today.

Another methodological issue is apparent with Svenson et al.'s (1999) Alberta study. These researchers claimed case ascertainment was high, as there are no disincentives for citizens in obtaining medical care and thus a diagnosis of MND in a publicly-funded health care system. Yet, individuals with MND may not seek medical care or a MND diagnosis, as they do not wish to learn they have a MND. In addition, they may wish to avoid some inevitable costs associated with obtaining health care. These costs include time spent in accessing health care services, which could mean a loss of income if these individuals need to take time away from paid employment. Costs in transportation and health care supplies are also absorbed by individuals, and may thus be another barrier to their receiving medical care, including obtaining a diagnosis of MND. Case ascertainment may thus not be as high as suggested by Svenson et al. One strength of this study, however, is that in 76% of the reported cases, a neurologist or neurosurgeon made the MND diagnosis, while in the remaining cases the diagnosis was made by a family physician.

Another methodological problem was apparent with Hudson et al.'s (1986) study. Although these researchers reviewed medical charts to confirm the MND diagnosis, this study was completed 20 years ago. Health information databases and research methods have developed since then – which indicates that MND rates may have changed. Regardless of these methodological and other issues, these Canadian findings provide a baseline of information about MND incidence, prevalence, and mortality rates.

Conclusion of Canadian MND Incidence, Prevalence, and Mortality Research Findings

As indicated, the incidence, prevalence, and mortality rates of MND have been researched in four separate Canadian provinces. Considerable variations in rates among the provinces are evident, with these possibly due to the methodological issues outlined rather than true differences in rates. Unfortunately, no information on the incidence, prevalence, and mortality rates of MND rates could be located for the Northern Territories, Quebec, Newfoundland, New Brunswick, Saskatchewan, Manitoba, and Prince Edward Island. Another issue is that the information collected for these four studies is dated, with the most recent article published 12 years ago. More current research is indicated, as rates may have increased or decreased in recent years. All such information is valuable to health services planning and health policy, in addition to indicating the types of research still needed to investigate and address MND.

International MND Incidence, Prevalence, and Mortality Research Findings

Incidence, prevalence, and mortality rates of MND have been researched in many countries throughout the world. The international research supplements the limited Canadian research and advances the understanding of incidence, prevalence, and mortality rates of MND. An overview of the international incidence, prevalence, and mortality rates of MND is provided below, followed by a discussion of a well-known cluster of MND, and a description of the highest and lowest reported incidence, prevalence, and mortality rates of MND. A discussion of the Canadian and international research including comparisons between the studies

and discrepancies or gaps in the literature follows.

International MND incidence, prevalence, mortality rates. From 1950 through 1983, MND was thought to have a uniform geographical distribution (Forsgen, Almay, Holmgren & Wall, 1983). More recently, it is thought that there is greater geographic variation (Annegers, Appel, Lee & Perkins, 1991). Changes in rates within countries are also becoming evident. In the United States, an increasing incidence of MND has been reported (Annegers, Appel, Lee & Perkins, 1991; Sorenson et al., 2002). Studies in Scotland have also suggested an increase in the incidence of MND (The Scottish Motor Neuron Research Group, 1992).

The most widely studied geographical clusters of MND have been in two west Pacific regions: West New Guinea and Guam (Salemi et al., 1989). A high incidence of MND has been frequently identified for these areas (Gajdusek & Salazar, 1982; Waring et al., 2004). However, it would also appear that the incidence of MND has been decreasing in these countries (Okumura, 2003; Plato et al., 2002; Spencer, Palmer & Ludolph, 2005). A high incidence and also prevalence rate of MND have similarly been reported for Scotland and Finland, while low rates have been reported for Mexico, Italy, Israel, and Hong Kong (Fong et al., 1996; Kahana & Ziber, 1984; Olivares, Esteban & Alter, 1972).

Although there may be undetected clusters of MND, two well-known clusters of MND have been repeatedly identified, both in the Western Pacific: West New Guinea and Guam (Yoshida et al., 1998). Although the incidence and prevalence rate of ALS in West New Guinea has decreased in recent years, it was among the highest in the world during the 1970s (Gajdusek & Salazar, 1982;

Spencer, Palmer & Ludolph, 2005). ALS was identified at that time as 100 times more common than anywhere else in the world (Steele & Guzman, 1987). More specifically, from 1975 through 1979, the crude average annual incidence rate of ALS in West New Guinea was 147 cases per 100,000 population (Gajdusek & Salazar). During this same time period, the prevalence rate in West New Guinea was 1,300 cases per 100,000 population (Gajdusek & Salazar). In contrast, the average annual crude incidence rate of ALS in Guam was 13 per 100,000 population in the period 1975 through 1979, a figure that is still high in comparison to the incidence of ALS in other countries (Waring et al., 2004).

Many studies suggested that the high incidence rate of ALS in the two Western Pacific countries were the result of a food source that is native to the area. As discussed in Chapter One, a researcher named Spencer reported that cycad seeds, a dietary staple for the Chamorros natives in Guam and commonly eaten in other parts of the West Pacific, resulted in the development of ALS (Steele & Guzman). The frequent consumption of these cycad seeds was thought to have caused toxicity and induced ALS (Steele & Guzman). Since this discovery, and with other diet changes with industrialization and modernization, the incidence rate has declined steadily (Garruto, Gajdusek & Chen, 1980; Garruto, Yanagihara & Gajdusek, 1985: Okumura, 2003; Plato et al., 2003; Waring et al., 2004) from 8 per 100,000 population from 1985 through 1989 (Waring et al.) to below 3 per 100,000 population in 1999 (Plato et al.). Prevalence and mortality rates were not investigated.

In addition to these two areas of high foci in the West Pacific, high incidence and/or prevalence rates of MND have also been reported for Japan, Scotland, and Finland. In a relatively recent study, Yoshida et al. (1998) found the crude average incidence rate of ALS in the Kii Peninsula of Japan was 1.43 per 100,000 population from 1989 through 1993. However, a higher incidence rate was reported for Japan by Kihira et al. (2005), who found the crude average annual incidence rate of ALS was 2.50 per 100,000 population from 1998 through 2002 (Kihira et al.). It is also notable that in 2002, they found the prevalence rate of ALS in Japan was 11.31 per 100,000 population (Kihira et al.). These variations in rates may be the result of improved diagnostic tools that have made a MND diagnosis more likely. It is also possible that more patients are seeking health care for MND symptoms (Kihira et al.). Another issue is that both studies involved data collection surveys sent to various hospitals and physician clinics; these survey tools differed. As such, underreporting of ALS cases could have occurred in both studies, or more so in one study than another. In addition, the incidence rates for both studies were calculated on small numbers of persons. Yoshida et al.'s study focused on 77 individuals with MND as compared to 215 individuals in Kihira et al.'s study.

High MND rates for Scotland have also been reported. Forbes, Colville, and Swingler (2004) found the crude incidence rate of ALS in Scotland was 7.5 per 100,000 population from 1989 through 1998. Furthermore, the prevalence rate of ALS in Scotland was established as 5 per 100,000 population in 1998 (Forbes, Colville & Swingler). Other researchers in Scotland reported the crude incidence rate of ALS in 1989 was only 2.24 per 100,000 population (The Scottish Motor

Neuron Research Group, 1992). These differences in rates may be due to different survey methods or research methods, as was the case for Japan. In Forbes, Colville, and Swingler's study, several different sources were accessed to obtain information on 1,226 individuals with MND over the nine-year study period. In the study conducted by The Scottish Motor Neuron Research Group, information was collected on only 123 individuals with MND. Both studies attempted to report on the entire population of individuals with MND, yet it is unlikely that entire populations were included in these studies.

High incidence, prevalence, and mortality rates of ALS have also been reported for Finland. Murros and Fogelholm (1983) reported that the average annual incidence rate of ALS in mid-Finland was 2.4 per 100,000 population from 1976 through 1981. The prevalence rate at that time was estimated at 6.4 per 100,000 population (Murros & Fogelholm). Maasilta, Jokelainen, Loytonen, Sabel, and Gatrell's (2001) study similarly found that the mortality rate of ALS in 1995 was 2.27 per 100,000 population in Finland.

In contrast, low incidence, prevalence, and mortality rates of MND have been reported for three countries: Mexico, Hong Kong, and Israel (Fong et al., 1996; Kahana & Zibler, 1984; Olivares, Esteban & Alter, 1972). The lowest incidence, prevalence, and mortality rates of MND were reported for Mexico, as the incidence rate of ALS was found to be 0.4 per 100,000 population and the prevalence rate was 1.44 per 100,000 population from 1968 through 1970 (Olivares, Esteban & Alter). During these years, the mortality rate of ALS was 0.28 per 100,000 population (Olivares, Esteban & Alter). In Hong Kong, low incidence

and mortality rates of MND were reported. During the years, 1989 through 1992, researchers reported the incidence of MND in Hong Kong was only 0.31 per 100,000 population and mortality rate of MND was 1.5 per 100,000 population (Fong et al., 1996). Similarly, a low incidence rate of MND was reported in Israel. During the years 1959 through 1974, the incidence rate of MND in Israel was 0.66 per 100, 000 population (Kahana & Ziber, 1984).

The Mexican, Hong Kong, and Israel studies cited above may not accurately reflect the true incidence, prevalence, and mortality rates of MND in these countries. In Mexico, the health care system was undeveloped in the 1960s and 1970s with MND cases likely to be undiagnosed (Olivares, Esteban & Alter). The Israel study based the incidence rate of MND on data collected in the 1950s, 1960s, and 1970s. As data collection and research methods have improved over the years, the incidence rate of MND in this study may not be a true measurement. Further research in Mexico, Hong Kong, and Israel would help understand the incidence, prevalence and mortality rates of MND in these low-risk countries, and as compared to Canada or other high-risk MND countries.

Discussion of MND Canadian and International Incidence, Prevalence, or Mortality Research Findings

The incidence, prevalence, and mortality rates of MND among the international research studies provide insight into how Canada compares with the rest of the world. The incidence and prevalence rates of MND reported in Murray et al's (1987) study and Svenson, Cwik, and Martin (1999) study reveals that, although Canada has not been recognized as having a high incidence or prevalence

of MND, MND may be more or less common in Canada as compared to some countries. While the highest incidence of MND in Canada was found to be 2.4 per 100,000 in Nova Scotia (Murray et al.) and the highest prevalence of MND in Canada was found to be 6.07 per 100,000 in Alberta (Svenson, Cwik & Martin), the average annual incidence rate of ALS for Finland was similarly 2.4 per 100,000 population and the prevalence rate was 6.4 per 100,000 population (Murros & Fogelholm). As discussed earlier, these studies have methodological concerns and are dated in that they reflect 1970s and 1980s data predominantly. Geographical variations may be due to research methodological issues primarily related to case ascertainment. Geographical variations may also reflect different standards for diagnosing MND, as well as different death certificate and other database variances, and different life expectancies, with longer life expectancies allowing more individuals who have acquired MND to reach an age where they exhibit disease symptoms (Giaheddu et al., 1993). However, these comparisons also raise the possibility that the incidence and prevalence rates, and mortality rates of MND in Canada are among the highest in the world. More recent and pan-Canadian research is required to better establish how MND compares to the rest of the world.

Conclusion of International MND Incidence, Prevalence, and Mortality Research Findings

Geographical variations in incidence, prevalence, and mortality rates of MND are evident in the literature. High incidence and prevalence rates in the Western Pacific have been clearly identified, with cycad seeds cited as the causative factor for these high rates. High rates have also been reported in other

areas of the world, particularly Japan, Scotland, Finland, and Canada. Low incidence, prevalence, and mortality rates of MND were reported for Mexico, Israel, Italy, and Hong Kong. These geographical variations in incidence, prevalence, and mortality rates may be reflective, however, of different research methods and improved case ascertainment over time rather than true variations in MND. Improved standards of diagnosis, improved death certificate documentation, and other factors also are responsible for these geographical variations.

Age-Related MND Research Findings

Age-related MND research has been conducted both in Canada and internationally. Research on the age at death from a MND provides an understanding of the life expectancy of Canadians who acquire a MND. Trend studies would also clarify whether the life expectancy with MND has increased or decreased over time, which would assist in planning health care and other support for persons with MND. Research could also clarify whether the life expectancy for males and females is generally the same or whether one gender lives longer than the other with MND. Age-based incidence, prevalence, and mortality rates also provide insight into the nature of this disease, such as whether it is age related.

The following section outlines the Canadian and international research investigating the age of MND decedents with regard to age-based incidence, prevalence, and mortality rates. A discussion of the research including comparisons among the studies, discrepancies in the literature and explanations for the discrepancies follows.

Canadian MND Mean Age at Death Research Findings

Three Canadian studies researched the mean age at death of individuals with MND. A south-western Ontario study conducted by Hudson, Davenport, and Hadler (1986) found the mean age at death from ALS in 1978-82 was 65.9 years of age for males and 68.0 years of age for females. Svenson et al.'s (1999) Alberta study found instead that the mean age of all MND decedents in 1994-95 was 66.2 years; or 64.6 years for males and 69.2 for females. Mandler et al.'s (2001) study of a combined sample of American and Canadian ALS decedents in 1997-2001 found their mean age at death was 62.0 years.

Discussion of Canadian MND Mean Age Death Research Findings

When reviewing the Canadian research on mean age at MND death, a few similarities and differences are apparent. Two of the three studies reported that females diagnosed with a MND live longer than males (Hudson et al. 1986; Svenson et al. 1999). According to Hudson et al., the mean age at death for females was 68 years, which was 2.1 years more than the mean age at death for males with ALS in this study. Similarly, Svenson et al's study found the mean age at death for females with MND was 69.2 years, which was 4.6 years more than the mean age at death for males with MND.

Hudson et al. (1986) and Svenson et al. (1999) also reported similar findings regarding the mean age at death. In Hudson et al.'s study, the mean age at death from ALS was 65.9; while in Svenson et al.'s study the mean age at death from MND was 66.2 years, a difference of only 0.3 years. This minimal difference is remarkable, as these studies were conducted 13 years apart. A related issue

regarding the mean age at death of MND decedents in Canada is revealed by Mandler et al.'s (2001) study that found the mean age at death of ALS decedents was 62.0 years. Although Mandler et al.'s study has the most recent data, it reflects the youngest mean age at death. Although a life expectancy increase could be anticipated, in keeping with a general increase in life expectancy in Canada, it appears that the life expectancy of persons diagnosed with MND has decreased over time.

However, the lower mean age found in Mandler et al.'s (2001) study may be a result of issues related to their sample. In Mandler et al.'s study, the sample was obtained through an ALS Patient Care Database. This is a voluntary database, where health care professionals collected information on end-of-life patterns of care by completing a one-page form consisting of 11 close-ended questions. For each ALS patient, this form was completed by one health care professional who interviewed the spouse or home health care provider following the patient's death. The 11 questions on the form gathered information regarding circumstances surrounding the patient's death. Among the 11 questions, none were on age at death. It is thus not known how the researchers in this study determined that the mean age at death from ALS was 62.0 years. Other important information was also not documented. For instance, although the researchers reported that 1,014 American and Canadians were included in the sample, they did not report how many were Canadians. Canadians findings were not reported separately, so as to be compared to American findings. Therefore, the findings in this study are less reflective of Canada, as ALS may affect Canadians differently than Americans.

Conclusion of MND Mean Age at Death Research Findings

The three studies that were completed in Canada on the mean age at death from MND, these found the mean age at death ranged from 62.0 years to 68.0 years. Two of these studies reported females live longer than males, however more recent population-based research is required to confirm this. Also, the most recent study reported that the mean age at death from ALS of a sample of Canadians and Americans combined was 62.0 years (Mandler et al., 2001), which suggested a possible decrease in age at death from MND over time. Further research is required to determine whether the mean age at death from MND has indeed been decreasing over time.

International MND Age at Death Research Findings

The age at death among individuals diagnosed with MND has been the subject of research in the United States, Italy, France, Finland, Japan, and Mexico. A total of 12 studies worldwide that investigated the mean age at time of death of individuals with MND were reviewed. Few of these investigated the mean ages at death for males and for females separately. Regardless, this information supplements the limited Canadian research into the mean age at death from MND. As such, the international research advances an understanding of the life expectancy with MND. This international research also helps in determining whether Canadians are unique or similar to other citizens.

The oldest mean age at death from MND was reported in Modena, Italy for the period 1990 through 1999 (Mandrioli, Faglioni, Merelli & Sola, 2003). During this time period, the mean age of death for males and females combined was 68.29

years. Okamoto et al.'s (2005) study in Japan similarly found that the combined mean age at death from ALS for both males and females was 67.8 years from 1995 through 2001. In contrast, the youngest mean age of death was reported in Mexico, using 1962 through 1969 data (Olivares, Esteban & Alter, 1972). In this early time period, researchers reported that the mean age of death from ALS for both males and females combined was 51.1 years.

Three international studies researched the mean age of death for males and for females separately, two of which found the mean age was higher for males than females. Olivares, Esteban, and Alter (1972) reported that females with ALS in Mexico had a younger mean age of death than males who died of ALS for the years 1962 through 1969. The mean age of death among females with ALS was 46.2 years, while the mean age of death among males was 56.0 years, a difference of 9.8 years (Olivares, Esteban & Alter). A study for Ferrara, Italy reported similar findings for the years 1964 through 1982, as the mean age of death among males with MND was 61.9 years, while the mean age of death for females with MND was 59.3 years, a difference of 2.6 years only (Granieri et al., 1988). A second Italian study found the mean age of death among females with ALS was higher than the mean age of death among males with ALS (Mandrioli, Faglioni, Merelli & Sola, 2003). For the years 1990 through 1999, the mean age of death among males with ALS was estimated as 67.67 years, while the mean age of death among females was 68.73 years, a difference of 1.06 years in favor of females (Mandrioli et al.). The finding that females live longer than males may be due to the unique population of Modena, Italy, as there is a high prevalence of elderly women there

(Mandrioli et al., 2003). Differences in life expectancy with gender, mobility patterns in countries, and health care seeking behaviors may explain such a unique finding for Modena, Italy. Regardless, this variance indicates that Canadian research is needed to establish whether females with MND live longer than males.

Discussion of Canadian and International MND Age at Death Research Findings

The international research has shown some variance in the mean age at death from MND, which could reflect health, health system, and data or data analysis issues. The international research also suggests a possible increasing mean age at death, as the most recent research reports have found the oldest mean ages at death from MND. Similarly, the youngest mean age at death from MND was reported in the oldest research study reviewed, as researchers reported in 1972 that the mean age at death from ALS was 51.1 years (Olivares, Esteban & Alter, 1972). Many factors could have supported an increase in age, although research method issues alone may be responsible for this increase in age. This latter issue is of considerable concern, as the Canadian research indicated that age at death was declining in Canada. As methodological issues were also apparent with the Canadian studies, it is not clearly evident whether people dying of MND are living longer now than in past decades.

The international and Canadian research studies, however, report a similar mean age at death from MND. For instance, in Modena, Italy the mean age at death from MND for males and females combined was 68.29 years in 2003 (Mandrioli, Faglioni, Merelli & Sola, 2003), which is similar to the mean age at death of 67.8 reported in 2005 for Japan (Okamoto et al., 2005). Both findings are similar to

recent Canadian findings, as in Alberta in 1994-95, the mean age at death from MND was 66.2 years (Svenson et al., 1999). A difference of only 1 or 2 years between Canadian means and those of other countries is apparent. The mean age at death in Canada from MND is therefore consistent with the research findings reported elsewhere. The mean age at death from MND can be viewed as typically resulting in a premature death, although most victims live to retirement age. Age at death has major implications for formal and informal support needs.

Additional comparisons can be made using the international and Canadian literature. Two international studies, that reported the mean age at death for males and females separately, reported that the mean age at death from MND for males was higher than the mean age at death from MND for females (Granieri et al., 1988; Olivares, Esteban & Alter, 1972). Two Canadian studies similarly reported that males had a higher mean age at death from MND than females (Hudson, Davenport & Hadler, 1986; Svenson et al., 1999). Although one international study found females lived longer than males, these studies indicate that Canada is similar to other countries with regard to gender-based MND outcomes. A population-based study of MND is needed to confirm this gender difference.

Conclusion of MND Mean Age at Death Research Findings

In recent international studies, the mean age at death from MND was found to be higher than for previous studies, thus indicating a possible trend toward an increased mean age at death. The majority of the internationally studies indicate the mean age at death from MND is between 67 and 69 years of age. Similarly, two of the three Canadian studies report the mean age at death from MND is between 64

and 69 years. The international and Canadian research both more commonly report that the mean age at death for males with MND is higher than the mean age at death for females with MND. The Canadian mean age at death findings are largely consistent with the international research findings.

Age-Based Incidence, Prevalence, and Mortality Research Findings

Age-based incidence, prevalence, and mortality rates of MND have been researched in Canada and internationally. The Canadian and international age-based incidence, prevalence, and mortality research finding are outlined below, along with a discussion of these findings.

Canadian MND Age-Based Incidence, Prevalence, and Mortality Research Findings

Three Canadian studies investigated age-based MND rates, although one focused on incidence, another on prevalence, and the third on mortality. Buchman et al.'s (1988) study found age-based incidence rates increased until the seventh decade of life and then subsequently declined after the seventh decade of life. Svenson et al. (1999) reported that there was an increased prevalence of MND with aging, although the specific age-based research findings were not reported. Instead of reporting by decade, they reported that there was an eight-fold increased risk of MND among persons aged 65 and older as compared to those under age 65. Hudson et al. (1986) also investigated age-based mortality rates of MND, and found the age-based mortality rate was highest in the 70 to 79 range. Specific age-rate findings were not documented.

International MND Age-Based Incidence Research Findings

Age-based MND incidence research has focused on Spain, Italy, Japan, Scotland, South Estonia, Texas, Hong Kong, Israel, Ireland, Denmark, Washington, Holland, Yugoslavia, Sweden, Finland, and Minnesota, (a U.S state). Most of these studies reported that the incidence of MND is either low or rare below 40 years of age (Annegers, Appel, Lee & Perkins, 1991; Forsgren, Almay, Holmgren & Wall, 1983; Giagheddu et al., 1993; Gross-Paju et al., 1998; Kahana & Zilber, 1984; Tysnes, Vollset & Aarli, 1991). Most of these studies also reported that the incidence rate of MND is higher at older ages, peaking in the sixth to eighth decade of life, and then declining afterward (Alcaz et al., 1996; Annergers, Appel, Lee & Perkins, 1991; Bettoni et al., 1994; Briani et al., 1996; Forsgren, Almay, Holmgren & Wall, 1983; Giagheddu et al., 1993; Govoni, Granieri, Capone, Manconi & Casetta, 2003; Gross-Paju et al., 1998; Hojer-Pedersen, Christensen & Jensen, 1989; Kihira et al., 2005; Kahana & Zilber, 1984; Logroscino et al., 2005; Mandrioli, Faglioni, Merelli & Sola, 2003; McGuire, Longstreth, Koepsell & van Belle, 1996; Murros & Fogelholm, 1983; Piemonte et al., 2001; Salemi et al., 1989; The Scottish Motor Neuron Research Group, 1992; Tysnes, Vollset & Aaril, 1991; Yoshidi et al., 1998). This age-based pattern of peaked incidence in the sixth to eighth decade of life with a decline thereafter is referred to as a pyramidal pattern of age distribution (Lopez-Vega, Calleja, Combarros, Polo & Berciano, 1988).

However, two studies reported a different age-based incidence pattern. Although the researchers in this more recent study did not actually report the incidence rates of MND in any age category, Lopez-Vega, Calleja, Combarros,

Polo, and Berciano (1988) found the incidence rate of MND in 1974 through 1984 for females in Cantabria, Spain increased with advancing age. A similar finding was reported through a study conducted for Rochester, Minnesota by Yoshida et al. (1986). This study revealed age-based incidence rates of ALS in 1925 through 1984 progressively increased with age and for both sexes. These researchers also did not report the incidence rates of ALS in any age category.

International MND Age-Based Prevalence Research Findings

Age-based prevalence rates of MND have been researched in three studies conducted in Italy, Ireland, and Texas. A pyramidal pattern, where the prevalence rate of MND reached a peak in mid life and then declined in older years was consistently reported (Annegers, Appel, Lee & Perkins, 1991; Mandrioli, Faglioni, Merelli & Sola, 2003; Traynor et al., 1999). More specifically, researchers reported for Modena Italy that the prevalence rate of ALS in 1989 through 1999 peaked in the age category of 75 to 79 years of age, at 15.66 per 100,000 population and then declined in the eighth decade of life (Mandrioli, Faglioni, Merelli & Sola). Traynor et al. reported similar findings for Ireland from 1995 through 1997, as the prevalence rate of ALS in Ireland was also found to increase with advancing age, reaching a peak between 65 and 84 years, and then declining after age 84. These researchers did not report the prevalence rate for specific age categories. Similarly, in Texas, the prevalence rates of MND from 1985 through 1988 were found to have increased with aging, as they peaked in the age category of 65 to 74 years and then declined after age 74 (Annegers et al.).

International MND Age-Based Mortality Research Findings

Age-based MND mortality rates have been researched in Finland, Norway, Spain, Italy, the United States, Japan, France, and England. All such reports indicated that mortality from MND is rare in persons 40 years of age or younger (Maasilta, Jokelainen, Loytonen, Sabel & Gatrell, 2001; Seljeseth, Vollset & Tysnes, 2000). In Finland, Norway, Texas, France, and Italy, researchers reported that the MND mortality rates increased with age, peaking in either the sixth, seventh, or eighth decade of life and then declining thereafter (Annegers, Appel, Perkins & Lee, 1991; Chio, Magnani & Schiffer, 1993; Durreleman & Alperovitch, 1989; Maasilta, Jokelainen, Loytonen, Sabel & Gatrell, 2001; Seljeseth, Vollset & Tysnes, 2000). Other researchers simply reported that mortality rates of MND in Spain, Japan, and England increase with age (Neilson, Robinson & Hunter, 1992; Okamoto et al., 2005; Veiga-Cabo, Almazan-Isla, Sendra- Gutierrez & Pedro-Cuesta, 1997).

Discussion of Canadian and International MND Age-Based Research Findings

The Canadian and international research on the age-based incidence, prevalence, and mortality rates of MND all indicated that MND is more common among older persons. However, most studies demonstrated an increased incidence, prevalence, and mortality from MND until a certain old age, with a decline thereafter. Given the fact that the three Canadian studies investigating age-based rates are dated, in that the most recent one was published 12 years ago, and that there are research method issues, additional research on age is indicated to clarify when MND deaths can be expected.

Only two of the international studies indicated that the incidence rates of MND (i.e. in Spain and the United States) did not decline, in later years but progressively increased with age (Lopez-Vega, Calleja, Combarros, Polo & Berciano, 1988; Yoshida et al., 1986). However, Yoshida et al.'s study is problematic, as this study only involved 44 individuals with MND. Lopez-Vega et al.'s study that reported similar age-based findings on 87 individuals with MND was similarly dated. Although these or other research issues may be responsible for this discrepancy in age-based findings, these studies raise the possibility that MND may be more common in the elderly than previously realized. Multiple health conditions that are common among elderly persons may complicate a diagnosis of MND (Yoshida et al., 1986).

Conclusion of MND Age-Based Rate Research Findings

International and Canadian research investigating age-based rates of MND report similar findings in general. The research indicates the incidence, prevalence, and mortality rates of MND increase with age until the older years and then subsequently decline. As before, research methodological issues could be the cause of differences in findings between studies and thus between countries. With only three dated studies having been completed in Canada, further research is obviously required to establish when MND deaths should be anticipated.

MND Gender-Based Research Findings

Gender-based MND incidence, prevalence, and mortality rates have been researched in many countries throughout the world. Canadian and international research investigating gender-based prevalence, incidence, and mortality rates are

outlined below. A discussion of this research, including a comparison of Canadian and international research, discrepancies in the literature, and explanations for the discrepancies follows. A review of the Canadian and international findings on gender-based incidence, prevalence, and mortality rates provides foundational knowledge for this thesis study. Gender-based differences are very common in most diseases, with some diseases more common to one gender or exclusive to that gender. Gender-based research findings thus provide relevant information for the detection, prevention, and treatment of a disease.

Canadian MND Gender-Based Research Findings

Three Canadian MND studies focus in whole or in part on gender distribution. The first published study was by Hudson, Davenport, and Hadler (1986). Their study investigated gender-based mortality rates in southwestern Ontario, Canada for the years 1978 through 1982. They reported that the peak mortality rate was 12.1 per 100,000 for men and 7.8 per 100,000 for women, giving a male to female ratio of 1.2:1 (Hudson et al.). These researchers also investigated gender-based MND prevalence rates. For the 139 persons who had a diagnosis of ALS in the four-year study period, 76 were males and 63 were females, making a gender ratio of 1.2:1.

The next study to be published was by Murray et al. (1987). Their study investigated the incidence rate of ALS in Nova Scotia for 1974-84. Over all years combined, more males were diagnosed with ALS than females, with a male to female ratio of 1.83 to 1.

MND prevalence rates in Alberta were investigated by Svenson et al. (1999). This study found the prevalence rate for 1994-95 was 8.9 per 100,000 population for males and 5.9 per 100,000 population for females, with an overall male to female ratio of 1 to 0.5.

International MND Gender-Based Research Findings

International studies supplement the limited Canadian research by providing additional understandings of gender-based information, including trends. Insights into how Canada compares to the rest of the world is understood by reviewing international studies. These additional gender-based incidence, prevalence, and mortality rates of MND are outlined below. A discussion, including a comparison among the international and Canadian studies, and explanations for discrepancies follows.

Gender-based incidence rates of MND internationally. While only one Canadian study investigated the incidence rate of ALS in Nova Scotia for 1974-84 (and found a male to female ratio of 1.83 to 1; Murray et al., 1987), gender-based MND incidence rates have been researched in Guam, Japan, Minnesota, Texas, France, Italy, Hong Kong, Germany, Denmark, Washington, South Estonia, Norway, Yugoslavia, Sweden, Scotland, Finland, Israel, and Ireland. Of the 31 studies that researched gender or sex-specific incidence rates of MND, only one indicated that MND is more common among females. This study in Finland found the annual incidence rate of ALS in 1976 was 2.0 per 100,000 population for males as compared to 2.8 per 100,000 population for females, making the gender ratio 1 male to 1.4 female (Murros & Fogelholm, 1983). All other studies found males had

a higher MND incidence rate as compared to females (Alcaz et al., 1996; Annergers, Appel, Lee & Perkins, 1991; Bettoni et al., 1994; Briani et al., 1996; Chazot, Vallat, Hugon, Lubeau & Dumas, 1986; Chazot, Vallat, Hugon, Lubeau & Dumas, 1987; Domenico et al., 1988; Forbes, Colville & Swingler; 2004; Forsgren, Almay, Holmgren, and Wall, 1983; Fong et al., 1996; Fong et al., 2005; Giagheddu et al., 1983; Giagheddu et al., 1993; Govoni, Granieri, Capone, & Manconi & Casetta, 2003; Granieri et al., 1988; Gross-Paju, et al., 1998; Hojer-Pedersen, Christensen & Jensen, 1989; Huber & Henn, 1995; Kahana & Zilber, 1984; Kihira et al., 2005; Logroscino et al., 2005; Lopez-Vega, Calleja, Combarros, Polo & Berciano, 1988; Mandriolo, Faglioni, Merelli & Sola, 2003; McGuire, Longstreth, Koepsell & van Belle, 1996; Okumura, 2003; Piemonte et al., 2001; Plato et al., 2003; Salemi et al., 1989; The Scottish Motor Neuron Research Group, 1992; Traynor et al., 1999; Tysnes, Vollset & Aaril, 1991; Waring et al., 2004; Yoshidi et al., 1998).

Most of the reviewed studies that showed MND was more common among males had similar findings. However, the greatest difference, however, in the incidence rate for males and females was reported for the Kii Peninsula of Japan (Yoshida et al., 1998). This study revealed the overall incidence rate of ALS from 1989 through 1993 was 2.23 per 100,000 population for males and 0.71 per 100,000 population for females, making the gender ratio 3.14 males to 1 female. Although the reasons for the significant male predominance of MND in the Kii Peninsula of Japan are unclear, this study was based on a total of 77 cases of MND. This small sample may not accurately reflect the true gender ratio neither in this

province nor in Japan.

Gender-based prevalence rates of MND internationally. While only one Canadian study focused on gender-based prevalence rates (which found the overall male to female ratio was 1 to 0.5; Svenson et al., 1999), international studies have more commonly researched the prevalence rates of MND for males and for females. These studies were conducted in Japan, Ireland, Germany, Italy, and Texas. All of these studies similarly reported that males had a higher prevalence rate than females. More specifically, in the eight studies that investigated the prevalence rates of MND for males and females, all found a higher prevalence among males (Annegers, Appel, Lee & Perkins, 1991; Giaggheddu et al., 1983; Granieri et al., 1988; Huber & Henn, 1995; Kihira et al., 2005; Mandrioli, Faglioni, Merelli & Sola, 2003; Salemi et al., 1989; Traynor et al., 1999). All eight studies reported that the difference in male and female prevalence rates was significant.

Seven of these reviewed studies had similar findings with regard to male/female prevalence. The largest difference in the prevalence rate of MND for males and for females was reported for Sardinia, Italy (Giagheddu et al., 1983). In 1970, the prevalence rate of ALS for males was 3.65 per 100,000 population while the prevalence rate of ALS for females was 0.94 per 100,000 population, making the ratio 3.88 males to 1 female for that year. This study only involved 182 actual cases of ALS, and thus may not be reflective of Italy as a whole nor Sardinia in previous or subsequent years.

Gender-based mortality rates of MND internationally. While only one Canadian study found a male to female morality ratio of 1.2 to 1 (Hudson et al.),

separate mortality rates for males and females were researched in 10 international studies. Among these 10 studies, 9 reported that males had a higher mortality rate of MND than females (Annegers, Appel, Perkins & Lee, 1991; Chio, Magnani & Schiffer, 1993; Durrleman & Alperovitch, 1989; Elian & Dean, 1992; Granieri et al., 1988; Okamoto et al., 2005; Riggs, 1990; Seljeseth, Vollset & Tysnes, 2000; Veiga-Cabo, Almazan-Isla, Sendra-Gutierrez & Pedro-Cuesta, 1997). The one study that reported the mortality rate of ALS was higher for females was completed in Finland (Maasilts, Jokelainen, Loytonen, Sabel & Gatrell, 2001). These Finish researchers reported that the ALS mortality rate from 1986 through 1995 for females in the over 65-age category was higher than the mortality rate of ALS for males in the same age group. However, these researchers did not report specific mortality rates.

Among the nine international studies that reported a high MND mortality rate for males, their findings were relatively similar. The largest difference, however, in MND mortality rates of MND for males and females was reported in Italy (Granieri et al., 1988). They found the mean MND mortality rate for the years 1964 through 1984 for males was 1.09 per 100,000 while the mean mortality rate for females was 0.61 per 100,000 population, making the gender ratio 1.78 males to every 1 female. In contrast, the gender ratio that was closest to unity was reported for Norway (Seljeseth, Vollset & Tysnes, 2000). These researchers found the ALS mortality rate for 1990-94 was 2.58 per 100,000 population for males and 2.50 per 100,000 population for females, a slight gender ratio difference of 1.03 to 1. These researchers indicated that an increased life expectancy among women placed

women in a higher risk age for acquiring ALS. However, the researchers claimed that the increased life expectancy among women compared with men is insufficient to fully explain the increase in mortality observed for women. Another reason may be the underreporting of ALS among women in previous years (Seljeseth, Vollset & Tysnes, 2000).

Discussion of International and Canadian MND Gender-Based Research Findings

The Canadian research, although minimal, consistently reported that males have a higher incidence, prevalence, and mortality rate than females. This finding is consistent with the international research, with the exception of a Finish study that found the incidence and mortality rates were higher among females (Maasilts et al., 2001). According to Maasilts et al. this unusual situation was due to the longer life expectancy for women than men in Finland. Thus, more females live to an age where MND is expressed. It would also seem possible that women are equally exposed as men in Finland to environmental toxins that may be contributing to developing a MND (Maasilts et al.).

Some international research also reports that mortality from MND is rare before the age of 40 (Maasilta et al., 2001; Seljeseth, Vollset & Tysnes, 2000). However, this information was not reported in the Canadian literature. Additional research is required to confirm this finding and other findings in Canada.

Conclusion of MND Gender-Based Research Findings

The Canadian and international literature clearly indicates, with few exceptions, that the incidence, prevalence, and mortality rates for MND are higher among males than females. Although this predominance among males is more

established in the international research, some limited Canadian research also supports the concern that males are more at risk of acquiring MND. With the last Canadian study published 12 years ago, it is possible that Canadian gender-based incidence, prevalence, and mortality rates may have changed. Research is indicated in Canada to establish if this predominance of MND among males has continued and increased or decreased.

MND Birthplace Research Findings

Although MND studies were conducted in many countries, none researched variances in incidence, prevalence, and mortality rates on the basis of multiple birthplaces. The birthplace of individuals with MND may be a key factor for the development of MND later in life, as some people may be exposed to a condition that results in MND while others are not. One benefit of Statistics Canada mortality data is that information on birthplace is available for analysis. This information may assist in revealing whether early conditions or influences in life are important for acquiring a MND.

MND Marital Status Research Findings

Only two studies have researched the marital status of individuals diagnosed with MND. The most recent was completed in Canada by Mandler et al. (2001), entitled *The ALS Patient Care Database: Insights into end-of-life care in ALS.* The other study was completed in South Estonia by Gross-Paju, K et al. (1998), entitled *Motor neuron disease in South Estonia.* Marital status is an important variable to research as it provides information about possible informal caregivers and the need for or use of formal health care services. With only one

Canadian study, the international study provides additional insights. A discussion of the findings of these research investigations follows.

Canadian MND Marital Status Research Findings

Mandler et al.'s (2001) study that primarily investigated end-of-life patterns of care and therapy for ALS patients in Canada and the United States examined data from an ALS patient care database. This is a voluntary database, consisting of information provided by health care professionals who completed a one-page survey form consisting of 11 closed-ended questions about 1,014 patients who died in the years 1997 through 2001. Although marital status was not the focus of the study, information was collected on this characteristic. Mandler et al. subsequently reported that 78.1% of the patients in this database were married, with their spouse the primary caregiver in 78.4% of cases. It was not reported whether the remaining 21.9% of patients in this database were single, divorced, or widowed. Mandler et al.'s study also revealed that, at the time of death, 76.8% of individuals diagnosed with ALS were living with their spouse, 9.7% were living alone, 2.2% were living with a friend, and 2.0% had "other" living arrangements.

International MND Marital Status Research Findings

A South Estonia study focused in part on investigating whether individuals at the time of their ALS diagnosis were living with their spouse or living alone (Gross-Paju et al., 1998). Among all 108 subjects, 57.4% were living with their spouse then. Unfortunately, the study did not reveal the actual marital rate among subjects. These researchers also reported more males than females were living with a spouse at the time of their diagnosis. Specifically, 75.9% of males and 37.5 % of

females were married and living with a spouse at the time of their diagnosis. These researchers also reported that more females than males were living alone at the time of diagnosis, as 0% of males and 12.5% of females were living alone at the time of their diagnosis.

Discussion of Canadian and International MND Marital Status Research Findings

The marital status findings of the Canadian study are similar to those of the international study, as both reported it was more common for persons with MND to be married than not married. With only two studies, one of which was completed outside Canada, it is obvious that more studies need to be conducted on martial status to establish if Canadians with MND are more commonly married or not. This information is highly relevant to the caregiving requirements that follow MND progression in severity.

In addition, future research should avoid the methodological problems that are apparent with these two studies. Gross-Paju et al.'s (1998) South Estonia study is problematic because the focus was on living arrangements as opposed to marital status. This study also only provided information on 108 persons who were referred to one hospital from 1985 to 1995, so the findings from this study cannot be generalized to that country as a whole, nor to Canada. Mander et al.'s (2001) Canadian study was based on interviews following the death of MND victims that health care providers had of spouses or home health care providers. A one-page survey form was completed after each interview, although routine visits had been made previously with patient, physician, and caregivers, with information also collected at those visits. It is not known when or how information on marital status

was collected, since none of the 11 questions on the one-page form asked about their marital status. Another problem is that among the 1,014 ALS subjects, information was not provided on the percentage of Canadian versus American subjects. The researchers did not report Canadian findings separately from American findings. Therefore, the findings of this study do not clearly inform the concern that a large proportion of Canadians who are living with MND may lack spousal or family support.

Summary of MND Marital Status Research Findings

Only two studies provided some information on marital status, one of which was in a European country. Although both showed persons with MND more often were married than not married, minimal information overall was provided. For instance, the length of marriage, the age or health of the spouse, and the existence or presence of children was not reported. In addition, information was not provided on the sex of the MND victim and spouse. It is possible that males with MND are more often married than females with MND, given the higher incidence of MND in males and the longer life expectancy of women. Furthermore, the other Canadian study combined both American and Canadian findings. As a result, the marital status of Canadians living with or dying of MND remains vague. The support needs of divorced and single persons could vary considerably from those of married persons.

Location of MND Death Research Findings

Among all reviewed research studies on MND, one study alone investigated the location of death among MND decedents (Mandler et al., 2001).

Mandler et al.'s study focused on end-of-life patterns of care and therapy for 1,014 ALS patients. Among these Americans and Canadians, 64.1% died at home, 20.7% died in hospital, 7.7% died in a nursing facility, and 6.9% died in a free-standing hospice. No other information was provided on location of death, such as length of care in these places or involvement of formal and/or informal caregivers.

Discussion of MND Location of Death Research Findings

Unfortunately, only one published study included information on location at death of MND decedents. There are several limitations with this study. One is that the researchers report 64.1% of the patients died at home on one-page and on another page the researchers report 66.6% of the patents died at home. Other issues regarding data collection are evident. Following the death, the health care provider interviewed the spouse or home health care provider and completed the one-page survey form. The researchers also reported that prior to the death, routine visits were made, and patient, physician, and caregiver data were collected. However, it is not known who made the routine visit and what type of data was collected or when. It is also not known how or when information regarding location of death was collected, as none of the 11 questions on the one-page survey form requested information on location of death. Also, among the 1,014 ALS decedents in the sample, the percentage of Canadians is not reported. The researcher did not report Canadian findings separately from Americans. Location of death may vary considerably between Canada and the United States, with considerable implications with regard to health care costs, and need for formal and informal supports near the time of death. This study, however, provides baseline data regarding the location of

death for MND decedents and is therefore important. Regardless, little is known about the location at death for MND decedents, and possible trends in location of death.

Conclusion of MND Location of Death Research Findings

As indicated above, only one study provided a small amount of information on location of death, information that indicated that more than half of MND deaths take place at home. This is a remarkable finding as it illustrates considerable need for informal and formal caregiving. More generally, this study indicates more research on location of death and trends in Canada are needed.

Conclusion to Chapter Two

The reviewed articles illustrated considerable differences across Canada and between Canada and other countries with regard to MND. Although research methodological issues are apparent, this body of research indicates that MND is more common in some countries than others. Although MND is relatively rare, MND may be as common in Canada as other high-incidence countries, although this possibility has not been previously recognized. It is possible that MND cases are increasing in Canada, with this a product of better data collection, immigration patterns, population aging, and other factors. MND is primarily a disease of mid to old age, with deaths commonly occurring after the age of retirement. The Canadian research also indicated a trend of people dying earlier from MND, which is a trend opposite to that found in other countries. Although only one study on gender was completed in Canada, MND consistently appears to be more common among males, yet this difference may be small or non-existent in Canada. Minimal

information is also available on marital status, birthplace, and location of death. Thus, this literature review indicates that additional studies, particularly age scale or population-based ones, are needed to provide evidence for health services and policy planning purposes.

CHAPTER THREE

Methodology

As indicated previously, the purpose of this thesis study was to examine pan-Canadian MND mortality data to determine whether MND is becoming more or less common and to explore other socio-demographic trends associated with MND. This chapter includes a discussion of the design, a description of the population, and definitions of terms used in the study. It also includes the plan that was implemented for analyzing the data, ethical considerations associated with this study, and an orientation to issues with death certificate data. Such that the limitations of this study are outlined as well as strengths.

Design

This study used a descriptive-comparative design to identify and compare annual MND prevalence and socio-demographic data for the years 1979 through 1999. The planning for this study's design was based on a literature review of previous Canadian MND research. International research also informed the planning for the study.

The questions addressed in this study were:

1. What are the overall and annual prevalence rates of MND in Canada, as based on national mortality data for the years 1979 through 1999?

2. What are the age trends among MND decedents in Canada for the years 1979 through 1999?

3. What are the gender trends of MND decedents in Canada for the years 1979 through 1999?

4. What birthplace trends, for those born within Canada or outside Canada, are notable among MND decedents in the years 1979 to 1999?

5. What are the trends in the marital status of MND decedents in Canada for the years 1979 through 1999?

6. What are the trends in province of residence for MND decedents that can be identified for the years 1979 through 1999?

7. What are the trends in hospital or non-hospital location of death for MND decedents in Canada for the years 1979 through 1999?

Sample/Population

The population that was examined in this study comprised all Canadian persons who were reported as having died of MND, as a primary cause of death, in the years 1979 through 1999. This population was a sub-set of a larger population of all decedents in Canada who had death certificate data recorded within the Statistics Canada mortality database over the same time period. Thus, this study did not involve a sample, as the entire group of persons who died of MND in selected years was studied. Studies involving an entire population are more accurate, as they avoid sampling error issues and other issues with using samples (Evans, 1998).

MND is classified as number 335 in the ICD-9-CM book that was published in 1980, and entitled *International Classification of Diseases, 9th Version, Clinical Modification. Volume 1, 2, and 3.* The ICD-9 classification system was in use from 1979 to 1999. As of 2000, the next classification version or (ICD-10) has been in use. Unfortunately, there are major differences in classifying diseases using ICD-9 versus ICD-10. The ICD-9 classification system was a

consistent method whereby all MNDs were identified by the number 335 each year over the study years, while the ICD-10 classification version introduced different numbers for various MNDs, and thus significantly changed how MND was classified. For reliability of data purposes, this study focused on the 21-year period when ICD-9 provided a consistent method for recording MND.

The number 335 is identified as Anterior Horn Cell disease in the ICD-9 book, with MND listed as a sub-category of Anterior Horn Cell disease. As defined in Chapter One, Anterior Horn Cell diseases are referred to as MND, as they are progressive degenerative diseases of the motor neuron (Krivickas, 2003). Anterior Horn Cell diseases include spinal muscular atrophy, ALS, and three ALS variants: Progressive muscular atrophy, primary lateral sclerosis, and primary bulbar palsy (Krivickas). Sub-categories of MND include ALS, progressive muscular atrophy, progressive bulbar palsy, pseudobulbar palsy, primary lateral sclerosis, and "other" motor neuron diseases.

Statistics Canada is a national organization that is based in Ottawa. This organization produces information that helps Canadians better understand their country; including it's people, resources, economy, society, and culture (Statistic Canada, 2006). Every five years, Statistics Canada completes a population census. As well, Statistics Canada manages approximately 350 active surveys on all aspects of Canadian life (Statistic Canada). Statistics Canada is also a database-holding agency, with one such database the Canadian mortality database.

The Statistics Canada mortality database contains pan-Canadian information that is a compilation of the information that is collected and forwarded by the

provinces and northern territories each year. The information that is compiled in the Statistics Canada mortality database originates from the death certificates that are completed in each respective province/territory. Annual death certificate information is converted into electronic format from a paper format and summarized before being sent to Statistics Canada each year. There were a number of sources of data error. The person completing the death certificate form may record incorrect information on the death certificate or not complete all required questions. Some death certificates may be lost and so no information is collected on some decedents. Another source of data error is random or systematic error when death certificate data is entered into a computer program or an electronic database. Data cleaning and data sharing processes (from province/territory to national organization or from national organization to researcher) are other methods by which data may be manipulated incorrectly or inappropriately, with data error thus inadvertently introduced. However, death certificate data are considered relatively reliable and valid (Chio et al., 1992), although some issues are important to highlight.

Issues with Death Certificate Studies

Completed death certificates contain information from medical certifiers who report the cause and medical circumstances of death (Hoyert & Lima, 2005). Medical certifiers are most often physicians, medical examiners, or coroners (Hoyert & Lima). Physicians can only certify natural deaths, while the medical examiner or coroner must make the final determination for suicides, homicides, or accidents such as drug overdoses and falls (Swain, Ward & Hartlaub, 2005). Each

medical certifier is required to complete information regarding the manner of death, the immediate cause of death, and the underlying cause of death. The manner of death is defined as the circumstances that surround the death such as suicide, homicide, or natural causes (Swain et al., 2005). The immediate cause of death is the most recently developed final diagnostic entity causing the death (Swain et al.). All such cases must have specific etiology, and not be a general concept, such as old age. Terms like cardiac arrest or organ failure that can have multiple etiologies are also to be avoided (Swain et al.). The medical certifier must also indicate the underlying cause of death. The underlying or primary cause of death is the fundamental or original diagnosis or condition from which the etiology occurs (Swain et al.). The description must be specific enough to clarify why the immediate causes of death developed (Swain et al.). MND would generally be considered the primary cause of death, while pneumonia would be a common immediate cause of MND death.

Mortality statistics derived from death certificate data compromise an available and inexpensive form of information about an entire population. However, there are issues regarding the reliability of data derived from death certificates. Physicians, medical examiners, and other person may not complete death certificate forms accurately or incompletely (Moussa et al., 1990). One of the most common and serious issues is that there may be one or more misdiagnoses on each death certificate (Chio, Magnani, Oddenino, Tolardo & Schiffer, 1992). For instance, alternative diagnoses to MND that appear on death certificates include multiple sclerosis, cancer, and cerebral vascular accident; all of which may suggest

low levels of physician knowledge regarding MND (Chio et al., 1992). False positive and false negative diagnoses have also been reported. In Finland, Jokelain (1977) found 4% to 8% of actual ALS cases were classified as non-ALS and that 6% of MND deaths were not really ALS cases (Jokelainen, 1977). Other errors in death certificates include an incorrect attribution of the immediate cause of death, listing causes in an incorrect or illogical manner, multiple competing immediate causes of death, poor match between cause and manner of death, and failure to identify the true underlying cause or causes of death (Swain et al., 2005). Another major limitation is that few variables are contained in large databases. The Statistic Canada database provided for analysis only includes the seven variables: Age, gender, cause of death, marital status, location-of-death, birthplace, and province of residence. An overview of each of the seven variables follows

Description of Statistics Canada Dataset Variables

1. Age. The variable "age" is the decedent's real or raw age, a discrete number that was recorded for each decedent at the time of death on the birth certificate. In each instance, this number is discrete and numeric, making this ratio or scale data. Deaths among persons under the age of one year of age were recorded in the dataset as zero (i.e. 0). Among the 9,028 persons who are designated as having MND in 1979 through 1999, age data were present in all 9,028 cases (0.0% missing data). Among the 4,030,010 persons who compromise the total population who died in Canada from 1979 through 1999, age data were missing in only 979 cases (0.02% missing data).

2. Gender. Gender or sex is a variable indicating whether each decedent was male or female. As with other death certificate data, the gender of the decedent should be recorded on the death certificate at the time of death. This variable provides information that is nominal in nature. Among the 9,028 persons who were identified as having died of MND in 1979 through 1999 all had gender data recorded (0% missing data). Among the 4,030,010 persons included in the total population who died from 1979 through 1999, in only eight cases were gender data missing (0.0% missing data).

3. Location of Death. Location of death is another variable recorded on the death certificate. The variable, location of death, is nominal in nature. It indicates whether the decedent died in hospital or a non-hospital location. Among the 9,028 persons who were identified as having died of MND in 1979 through 1999, all had location of death recorded (0% missing data). Among the 4,030,010 persons included in the total population who died from 1979 through 1999, 228,467 cases had location of death data missing (5.6% missing data).

4. Cause of Death. The primary cause of death is also recorded on death certificates. The variable, cause of death, is nominal. The ICD number 335 indicates that the decedent died of MND, while all other numbers indicate that they did not die of MND. As indicated above, a total of 9,028 persons were identified as having died of MND in the years 1979 through 1999. Among the 4,030,010 persons included in the total population who died from 1979 through 1999, the cause of death was missing in only 65 cases (0.0% missing data).

5. Marital Status. Each decedent's marital status is also recorded on the death certificate. The variable "marital status" is nominal in nature. This variable indicates whether the decedent was married or not at time of death. Among the 9,028 persons who were identified as having died of MND in 1979 through 1999, marital status was missing in only 52 cases (0.0% missing data). Among the 4,030,010 persons included in the total population who died from 1979 through 1999, martial status information was missing in 33,753 cases (0.8% missing data).

6. Birthplace. Each decedent's birthplace should also be recorded on the death certificate. The variable "birthplace" is nominal in nature. This nominal data indicates whether the decedent was born in Canada or not born in Canada. Among the 9,028 persons who were identified as having died of MND in 1979 through 1999, birthplace data were missing in 592 cases (6.6% missing data). Among the 4,030,010 decedents included in the total population who died from 1979 through 1999 martial status was missing in 438,911 cases (10.1% missing data).

7. Province of Residence. Each decedent's province of residence is expected to be recorded on their death certificate. The variable "province of residence" is nominal, indicating which province the decedent was resided in at the time of their death. Among the 9,028 persons who were identified as having died of MND in 1979 through 1999, all had province of residence recorded (0% missing data). Among the 4,030,010 decedents included in the total population who died from 1979 through 1999, in 438,911 cases, province of residence data were missing (10.1% missing data).

Data Analysis

The data analysis was designed to answer each of the seven research questions.

1. What is the prevalence rate of MND in Canada, as determined by national mortality data for the years 1979 through 1999? This question was answered by counting the number of persons who are designated as having MND (using number 335 in the disease variable column) over all years combined and in each year as compared to the total number of persons who died in other years. The overall gross prevalence rate of MND over all years combined was calculated as 224.02 per 100,000 deceased persons. Changes in the annual rate of MND were compared over the 21 study years using the chi-square test. As indicated in the following definition of terms section, the chi-square test is an appropriate test to use when the variables are nominal, as opposed to ordinal or scale in nature.

2. What are the age trends among MND decedents in Canada for the years 1979 through 1999? This question was answered by comparing the mean age of all persons who died of MND each year, using the ANOVA test. In addition, a Pearson correlation test was used to compare annual trends in decedent ages over the 21-year period and combined.

3. What are the gender trends of MND decedents in Canada for the years 1979 through 1999? This question was answered by counting the number of females and the number of males who are designated as having died of MND (using the number 335 in the disease variable column) each year and describing them using simple descriptive percentages over all years combined and for each

year. A male-female ratio for each year and over all years combined were manually calculated. The male versus female distribution for each year was also compared over the 21 years using the chi-square test. As indicated in the following definition of terms section, the chi-square test is an appropriate test to use when the variables are nominal as opposed to ordinal or scale in nature.

4. What birthplace trends for those born within Canada or outside Canada are notable among MND decedents for years 1979 to 1999? This question was answered by counting and comparing the number of persons born in Canada and outside Canada who are designated as having died of MND (using the number 335 in the disease variable column), with a rate/percentage for all years combined and for each year then calculated. Changes in these proportions were then compared over the 21 years using the chi-square test. As indicated in the following definition of terms section, the chi-square test is an appropriate test to use when the data variables are nominal as opposed to ordinal or scale in nature.

5. What marital trends of MND decedents in Canada are notable for the years 1979 through 1999? This question was answered by counting the number of persons who are designated as having MND (using the number 335 in the disease variable column) each year who were recorded as married or not married. A rate/percent was then determined for each year and for all years combined. Marital status is attributions were then compared over the 21 years using the chi-square test. As indicated in the following definition of terms section, the chi-square test is an appropriate test to use when the variables are nominal as opposed to ordinal or scale in nature.

6. What provincial trends in MND decedents can be identified for the years 1979 through 1999? This question was answered by counting the number of persons who were designated as having MND (using the number 335 in the disease variable column) each year by province. A province-specific rate/percent overall years combined and for each was then calculated and the chi-square test used to determine if changes in provincial residence counts had occurred over time. A Chi-square test for each province was conducted, to assess if the prevalence of MND cases increased or decreased over the 21 years within each respective province. As indicated in the following definition of terms section, the chi-square test is an appropriate test to use when the variables are nominal as opposed to ordinal or scale in nature.

7. What trends in hospital or non-hospital location of death for MND decedents in Canada can be noted for the years 1979 through 1999? This question was answered by counting the number of persons who were designated as having died of a MND (using the number 335 in the disease variable column) each year who died in hospital and those who died in a non-hospital location. The all-years combined and annual rate/percent were then calculated. This location of death data was then compared over the 21 years using the chi-square test. As indicated in the following definition of terms section, the chi-square test is an appropriate test to use when the variables are nominal as opposed to ordinal or scale in nature.

Definition of Terms

There are several important terms that needed clarification for planning and operational purposes. These include definitions of the statistical tests that were

performed in this thesis study.

Chi-square. The chi-square test is a non-parametric test of statistical significance for bivariate tabular analysis, also known as crossbreaks (Chi-Square, 2006) or cross tabs. Bivariate tabular (crossbreak/crosstab) analysis is used when trying to summarize the intersections of independent and dependent variables, and understand the relationship (if there is any) between typically nominal variables (Chi-Square). Typically, the hypothesis tested with chi-square is whether or not two samples are different enough on some characteristic or aspect (Chi-Square). The Chi-square test is a rough estimate of confidence because it accepts weaker, less accurate data as input and therefore has less status in the pantheon of statistical tests (Chi-Square). However, its limitations are also its strengths because chi-square is more "forgiving" in the data it will accept. As such, this test can be used in a wide variety of research contexts (Chi-Square).

T-test. The t-test assesses whether the means of two groups are statistically different from each other. This analysis is appropriate for comparing the mean scores of two groups (t-test, 2006). As such, ratio or scale data are needed for t-test analysis.

Pearson Correlation. A correlation between two variables reflects the degree to which the two variables are related. Pearson's correlation reflects the degree of linear relationship between two interval or scale variables. It ranges from +1 to -1. A correlation of +1 means that there is a perfect positive linear relationship between variables (Pearson correlation, 2006)

ANOVA. Analysis of variance is a statistical test used to evaluate the

significance of differences between the mean scores of two or more groups (Evans, 1998). It is similar to the t-test in this regard, but different from the t-test in that the mean scores of many groups can be compared as opposed to just two mean scores.

Ethical Considerations

Ethical approval for this thesis study, and other mortality trend studies, using the Statistics Canada 1950 through 2000 data that were provided by Statistic Canada to Dr. Wilson, was granted by the University of Alberta, Health Research Ethics Approval Board in June 2006. This research ethics approval expires June 2007 (see approved letter in attached Appendix A).

As this is a secondary analysis, consent was originally obtained for the use of these data from Statistics Canada. Please note that the Statistics Canada website states: "We are committed to protecting the confidentiality of all information entrusted to us" (Statistics Canada). The Statistic Canada database does not include any names, numbers, or any other identifying characteristics, to protect individual decedent anonymity and confidentiality of information. No adverse effects from this thesis study were expected, nor appeared to have occurred during this study. This thesis study is beneficial, as few Canadian studies have investigated MND mortality and other trends. This study increases the current knowledge base on MND in Canada, thereby provided greater insight into how this disease affects Canadians.

CHAPTER FOUR

Findings

As indicated earlier, the purpose of this thesis study was to examine mortality trends of MND in Canada to determine if MND is becoming more or less common and to explore other socio-demographic trends associated with MND. Seven specific research questions were developed to guide this research investigation, and this chapter provides the findings for each of these questions. Research approval for this study and others involving the Statistics Canada mortality data was provided by the University of Alberta Health Research Ethics Board to Dr. Donna Wilson in June 2006, with this ethical approval valid for one year. The student's thesis committee, as proposed, approved this study, on July 28, 2006.

As outlined earlier, the data for this study were originally supplied by Statistics Canada to Dr. Wilson. A subset of this data was provided to the student on August 1, 2006. This data file was analyzed during the month of August 2006 using the SPSS (version 14.0) computer program. This program was loaded, along with the data subset, on a password-protected computer in a locked office. The data received consisted of select death certificate information all Canadian persons who died in the years 1979 through 1999, including all Canadians who were reported as having died of MND in those years (i.e. ICD-9 cause of death # 335). This study did not involve a sample, as the entire group of persons who died of MND in these years was studied.

Findings For Each Research Question

Question One

What is the prevalence rate of MND in Canada, as determined by national mortality data for the years 1979 through 1999?

Over all years combined, 0.2% of all decedents in 1979 through 1999 died of MND. More specifically, 9,028 persons were recorded as having died of MND out of a total 4,03,0010 persons in these years. The least number of annual reported cases of MND was 299 persons in 1979, the first year. A general increase over time was noticed in the number of annual reported cases, with 526 persons reported as having died of MND in 1999, the last year (see Table 1).

Table 1. MND Decedents and Other Decedents: 1979-1999

Year	MND N (%)	All Other Diseases N (%)	Total N (%)
1979	299 (0.2)	167,172 (99.8)	167,471 (100)
1980	316 (0.2)	170,411 (99.8)	170,727 (100)
1981	307 (0.2)	170,007 (99.8)	170,314 (100)
1982	313 (0.2)	173,618 (99.8)	173,931 (100)
1983	352 (0.2)	173,462 (99.8)	173,814 (100)
1984	364 (0.2)	174,772 (99.8)	175,136 (100)
1985	370 (0.2)	180,402 (99.8)	180,772 (100)
1986	392 (0.2)	183,260 (99.8)	183,652 (100)
1987	422 (0.2)	183,981 (99.8)	184,403 (100)
1988	406 (0.2)	189,252 (99.8)	189,658 (100)
1989	439 (0.2)	190,013 (99.8)	190,452 (100)
1990	396 (0.2)	191,356 (99.8)	191,752 (100)
1991	429 (0.2)	194,896 (99.8)	195,325 (100)
1992	481 (0.2)	195,637 (99.8)	196,118 (100)
1993	528 (0.3)	203,972 (99.7)	204,500 (100)
1994	509 (0.2)	206,292 (99.8)	206,801 (100)
1995	541 (0.3)	209,858 (99.7)	210,399 (100)
1996	565 (0.3)	211,967 (99.7)	212,531 (100)
1997	539 (0.3)	214,827 (99.7)	215,366 (100)
1998	535 (0.2)	217,177 (99.8)	217,712 (100)
1999	526 (0.2)	218,650 (99.8)	219,176 (100)
Total	9,028	4,020,982	4,030,010

Significant Value: $x^2 = 130.028$, df = 20, p = 0.000

Through chi-square analysis, a significant difference was found in the annual count of MND count as compared to all other diseases causing death for the years 1979 through 1999 ($x^2 = 130.028$, df = 20, p = 0.000). Over time, the proportion or percentage rate of MND to all other causes of death increased slightly. In most years, however, only 0.2% of all deaths were from MND. In more recent years, this increased to 0.3%. In the first 14 years, an annual rate of 0.2% was found. In 1993, 1995, 1996, and 1997; 0.3% of all deaths were recorded as having been from MND.

Based on these data, the overall gross prevalence rate of MND over all years combined was calculated as 224.02 per 100,000 deceased persons. In the first year, 1979, the prevalence/mortality rate was 178.54 per 100,000. In 1999, the prevalence rate of MND was 239.99 per 100,000 persons. Thus, there was a slight increase over time in the gross prevalence/mortality rate of MND. This increase corresponds with the small proportional increase in cases over time.

Question Two

What are the age trends among MND decedents in Canada for the years 1979 through 1999?

Among the 9,028 people who were recorded as having died of MND, a slight but significant increase in average annual age was noted from 1979 through 1999 (see Table 2). This significant difference was found using ANOVA, which compared the mean age of persons who died each year of MND from 1979 through 1999 (F = 2.417, df = 20, p = 0.000). In 1979, the mean age at death was 61.7 years while in 1999, the mean age at death was 65.79 years. Over all 21 years combined,

the average age at death was 64.3 years (Median = 68 years, Multiple modes = 70, 71, and 72, SD = 17.552, Range = 0 -100).

Using the Pearson one-tailed correlation test, a significant positive correlation (although weak) was also found, as calculated on the basis of age at death for all persons who were recorded as having died of MND and their year of death ($R = 0.063$, $p = 0.000$). This test similarly demonstrated that the average age of MND decedents had increased over time.

As mentioned, among the 9,028 people who were recorded as having died of MND, a slight but significant increase in average annual age was noted from 1979 through 1999 (see Table 2). A significant difference in age at death among MND decedents and decedents of all other causes of death was found ($t = -30.8$, $df = 4,029,379$, $p = 0.000$). Over all 21 years combined, the average age at death from MND was 64.3 years as compared to 70.5 years for all other causes of deaths.

Table 2. MND Decedent Age Trends: 1979-1999

Year	N	Mean	Std. Deviation	95% Confidence Interval for Mean	
				Lower Bound	Upper Bound
1979	299	61.70	18.512	59.60	63.81
1980	316	62.01	17.343	60.09	63.93
1981	307	61.70	18.490	59.62	63.78
1982	313	62.99	17.574	61.04	64.94
1983	352	63.18	18.367	61.26	65.11
1984	364	63.90	17.132	62.14	65.67
1985	370	62.57	18.159	60.71	64.43
1986	392	63.62	18.112	61.82	65.42
1987	422	63.59	17.933	61.88	65.31
1988	406	64.16	19.347	62.27	66.05
1989	439	64.81	17.893	63.13	66.49
1990	396	65.35	17.858	63.58	67.11
1991	429	65.25	18.440	63.50	67.00
1992	481	65.04	17.223	63.49	66.58
1993	528	65.59	16.239	64.20	66.97
1994	509	63.62	17.935	62.06	65.18
1995	541	64.72	17.316	63.26	66.19
1996	564	66.07	15.300	64.80	67.33
1997	539	65.35	17.244	63.89	66.80
1998	535	65.40	17.256	63.93	66.86
1999	526	65.79	16.172	64.41	67.18
Total	9,028	64.34	17.552	63.98	64.70

Significant Value: $F = 2.417$, $df = 20$, $p = 0.000$; $R = 0.063$, $p = 0.000$

Question Three

What are the gender trends of MND decedents in Canada for the years 1979 through 1999?

Although 52.4% of all persons who died of MND over the 21 years were male, in five relatively recent years (1987, 1993, 1994, 1996 and 1997), more than 50% of MND cases each year were female (see Table 3). A significant difference in gender distribution over time among MND decedents was found ($x^2 = 34.871$, $df = 20$, $p = 0.021$). That is an increase over time in female cases was found.

Regardless, in 16 of the 21 years (1979 through 1986, 1988 through 1992, 1995, and 1998 through 1999) more males than females died of MND. In the first year (1979), 56.9% of all cases were male and in the last year (1999) 55.5% of all cases were male. A slight increase in female cases occurred proportionally over time. The ratio over all years combined was 1.1 males to every 1.0 female. In the first year (1979), the ratio was 1.3 males to 1.0 female and in the last year (1999) this ratio was 1.2 male to 1.0 female

Table 3. MND Decedent Gender Trends: 1979-1999

Year	Gender		Total N (%)
	Male N (%)	Female N (%)	
1979	170 (56.9)	129 (43.1)	299 (100)
1980	177 (56.0)	139 (44.0)	316 (100)
1981	156 (50.8)	151 (49.2)	307 (100)
1982	172 (55.0)	141 (45.0)	313 (100)
1983	206 (58.5)	146 (41.5)	352 (100)
1984	192 (52.7)	172 (417.3)	364 (100)
1985	200 (54.1)	170 (45.9)	370 (100)
1986	213 (54.3)	179 (45.7)	392 (100)
1987	208 (49.3)	214 (50.7)	422 (100)
1988	207 (51.0)	199 (49.0)	406 (100)
1989	221 (50.3)	218 (49.7)	439 (100)
1990	213 (53.8)	183 (46.2)	396 (100)
1991	226 (52.7)	203 (47.3)	429 (100)
1992	254 (52.8)	227 (47.2)	481 (100)
1993	262 (49.6)	266 (50.4)	528 (100)
1994	251 (49.3)	258 (50.7)	509 (100)
1995	290 (53.6)	251 (46.4)	541 (100)
1996	264 (46.8)	300 (53.2)	564 (100)
1997	258 (47.9)	281 (52.1)	539 (100)
1998	300 (56.1)	235 (43.9)	535 (100)
1999	292 (55.5)	234 (44.5)	526 (100)
Total	4,732 %	4,296 %	9,028

Significant Value: $x^2 = 34.871$, df = 20, p = 0.021

Question Four

What birthplace trends for those born within Canada or outside Canada are

notable among MND decedents for the years 1979 to 1999?

In the first year (1979), 76.6% of MND decedents were born in Canada as compared to 75.0% in the last year (1999) (See Table 4). When Canadian versus non-Canadian birthplace among MND decedents was compared over time, a significant difference was not found using chi-square analysis ($x^2 = 26.271$, df = 20, p = 0.157). Over all years combined, 76.3% of MND decedents were born in Canada and 23.7% were born outside of Canada. In each year, from 1979 through 1999, over 68% of all MND decedents were born in Canada.

Table 4. MND Decedent Birthplace Trends: 1979-1999

Year	Born in Canada or Not		Total N (%)
	Canadian N (%)	Other N (%)	
1979	131 (76.6)	40 (23.4)	171 (100)
1980	200 (68.3)	93 (31.7)	293 (100)
1981	220 (76.9)	66 (23.1)	286 (100)
1982	200 (74.9)	67 (25.1)	267 (100)
1983	250 (79.6)	64 (20.4)	314 (100)
1984	255 (77.0)	76 (23.0)	331 (100)
1985	266 (74.3)	92 (25.7)	358 (100)
1986	289 (76.3)	90 (23.7)	379 (100)
1987	309 (75.0)	103 (25.0)	412 (100)
1988	297 (74.4)	102 (25.6)	399 (100)
1989	319 (79.9)	80 (20.1)	399 (100)
1990	291 (77.0)	87 (23.0)	378 (100)
1991	324 (79.8)	82 (20.2)	406 (100)
1992	357 (78.3)	99 (21.7)	456 (100)
1993	389 (77.2)	115 (22.8)	504 (100)
1994	381 (78.9)	102 (21.1)	483 (100)
1995	402 (76.6)	123 (23.4)	525 (100)
1995	404 (75.4)	132 (24.6)	536 (100)
1997	373 (73.7)	133 (26.3)	506 (100)
1998	390 (76.5)	120 (23.5)	510 (100)
1999	392 (75.0)	131 (25.0)	523 (100)
Total	6,439 (76.3)	1,997 (23.7)	8,436 (100)

Significant Value: $x^2 = 26.271$, df = 20, p = 0.157

Question Five

What marital trends of MND decedents in Canada are notable for the years 1979 through 1999?

Over all years combined, 63.2% of MND decedents were married and 36.8% were not married. In each year, from 1979 through 1999, over 58% of MND decedents were recorded as married at the time of their death (see Table 5). In the first year (1979), 58.7% of MND decedents were married as compared to 63.2% in the last year (1999), a relatively minor difference. When the married versus not married status of MND decedents was compared over time, a significant difference was not found using chi-square analysis ($x^2 = 15.282$, df = 20, p = 0.760).

Table 5. MND Decedent Marital Trends: 1979-1999

Year	Married or Not Married		Total N (%)
	Married N (%)	Not Married(%)	
1979	175 (58.7)	123 (41.3)	298 (100)
1980	201 (64.0)	113 (36.0)	314 (100)
1981	197 (64.6)	108 (35.4)	305 (100)
1982	208 (66.7)	104 (33.3)	312 (100)
1983	227 (64.7)	124 (35.3)	351 (100)
1984	239 (66.2)	122 (33.8)	361 (100)
1985	231 (62.8)	137 (37.2)	368 (100)
1986	254 (65.0)	137 (35.0)	391 (100)
1987	266 (63.0)	156 (37.0)	422 (100)
1988	247 (60.8)	159 (39.2)	406 (100)
1989	264 (60.3)	174 (39.7)	438 (100)
1990	252 (63.6)	144 (36.4)	396 (100)
1991	262 (61.4)	165 (38.6	427 (100)
1992	302 (62.9)	178 (37.1)	480 (100)
1993	312 (59.8)	210 (40.2)	522 (100)
1994	331 (65.2)	177 (34.8)	508 (100)
1995	341 (63.4)	197 (36.6)	538 (100)
1995	347 (61.6)	216 (38.4)	563 (100)
1997	347(65.2)	185 (34.8)	532 (100)
1998	337 (63.5)	194 (36.5)	531 (100)
1999	331 (64.1)	185 (35.9)	516 (100)
Total	5,671(63.2)	3,308 (36.8)	8,976 (100)

Significant Value: $x^2 = 15.282$, df = 20, p = 0.760

Question Six

What provincial trends in MND decedents can be identified for the years 1979 through 1999?

Over all years combined, 10 provinces and territories among all 12 had an overall 21-year rate of 0.2% of MND cases among decedents in those provinces or territories, while two provinces or territories (British Columbia and Yukon territory) had an overall 21-year combined rate of 0.3% (see Table 6). Using chi-square analysis, this difference in provincial MND cases versus other cases was significant (x = 51.048, df = 11, p = 0.000).

Table 6. MND Decedent Province of Residence Trends: 1979-1999

Province of Residence	Motor Neuron Disease or Not		Total N (%)
	Motor Neuron Disease N (%)	All Other Diseases N (%)	
Prince Edward Island	56 (0.2)	23,142 (99.8)	23,198 (100)
Nova Scotia	323 (0.2)	154,521 (99.8)	154,844 (100)
New Brunswick	243 (0.2)	116,279 (99.8)	116,522 (100)
Quebec	2,252 (0.2)	1,011,371 (99.8)	1,013,623 (100)
Ontario	3,199 (0.2)	1,483,777 (99.8)	1,486,976 (100)
Manitoba	407 (0.2)	187,879 (99.8)	188,286 (100)
Saskatchewan	362 (0.2)	169,781 (99.8)	170,143 (100)
Alberta	724 (0.2)	299,710 (99.8)	300,434 (100)
British Columbia	1,290 (0.3)	489,032 (99.7)	490,322 (100)
Yukon	8 (0.3)	2,564 (99.7)	2,572 (100)
Northwest Territories	9 (0.2)	5,009 (99.8)	5,018 (100)
Newfoundland	155 (0.2)	77,917 (99.8)	78,072 (100)
Total	9,028 (0.2)	4,020,982 (99.8)	4,030,010 (100)

Significant Value: $x^2 = 51.048$, df = 11, p = 0.000

In three provinces, Quebec, Ontario, and Alberta, a significant change over time in the proportion of cases of MND as compared to the proportion of all other causes of death in each province was found using chi-square analysis (See Table 7). More specifically, in Quebec, a significant difference over time in MND disease rates versus all other causes of death was found using chi-square analysis

($x^2 = 85.987$, df = 20, p = 0.000), with a slight increase in the MND rate - from 0.2% of deaths in the first year (1979) attributed to MND as compared to 0.3% in the last year (1999) evident. In Ontario a significant difference was also found using chi-square analysis ($x^2 = 51.670$, df = 20, p = 0.000), with a slight but minimal increase in MND, as the rate of MND was 0.2% in both the first and last years. In 1995, 0.3% of all deaths in Ontario were attributed to MND. In Alberta, a significant difference was also found ($x^2 = 36.687$, df = 20, p = 0.013). This change was a minimal but variable increase over time, as the provincial rate of MND was 0.2% in both the first and last years. In 1997 and 1998, 0.3% of all deaths in Alberta were attributed to MND.

In contrast, significant differences over time in the proportion of MND as compared to all other diseases causing death combined were not found for each of the remaining nine provinces and territories. More specifically, in Prince Edward Island, a significant change over time in MND versus all other causes of death was not found ($x^2 = 22.978$, df = 20, p = 0.290). Although 0.0% of deaths in Prince Edward Island were attributed to MND in the first year (1977) as compared to 0.4% in the last year (1999), there were a very small number of cases of MND each year (under 5 per year) that likely explains this non-significant chi-square test. In Nova Scotia, there was similarly not a significant change in MND versus all other causes of death over time ($x^2 = 28.513$, df = 20, p = 0.098), although in the first year (1979) 0.1% deaths were attributed to MND as compared to 0.3% in the last year (1999). Small case numbers and variable rates may also explain this non-significant difference. In New Brunswick, a significant change in MND cases versus all other

cause of death cases over time was also not found ($x^2 = 28.038$, df = 20, p = 0.109), likely as 0.2% of deaths in both the first (1979) and last years (1999) were attributed to MND. In Manitoba, a significant change in MND cases versus all other cause of death cases over time was not found ($x^2 = 18.144$, df = 20, p = 0.578), with 0.2% of all provincial deaths in the first year (1979) and last year (1999) attributed to MND. In Saskatchewan, a significant change in MND cases versus all other cause of death cases over time was also not found ($x^2 = 15.535$, df = 20, p = 0.745), likely because 0.2% of all provincial deaths in the first year (1979) and last year (1999) were attributed to MND. In British Columbia, a significant change in MND cases versus all other cause of death cases over time was also not found ($x^2 = 18.122$, df = 20, p = 0.579), with 0.2% of provincial deaths in the first year (1979) and last year (1999) attributed to MND. In the Yukon Territory, a significant change in MND cases versus all other cause of death cases over time was also not found ($x^2 = 13.281$, df = 20, p = 0.865). Although in 1979, 0.8% of all Yukon Territory deaths were attributed to MND as compared to 0.7% in the last year (1999), only a very small number of cases of MND deaths were recorded each year (under 2 per year). This small number each year, and the random presentation of annual cases is likely the reason for a non-significant finding. In the Northwest Territories, a significant change in MND cases versus all other cause of death cases over time was also not found ($x^2 = 25.345$, df = 20, p = 0.189). This finding may be because the rate of MND was 0.0% in both the first (1979) and last years (1999). In Newfoundland, a significant change in MND cases versus all other cause of death cases over time was also not found ($x^2 = 18.761$, df

= 20, p = 0.537). Although 0.2% of deaths were attributed to MND in the first year (1979) as compared to 0.1% in the last year (1999), the non-significant chi-square finding may reflect the small annual number and fluctuations in cases of MND each year (under 12 per year).

Table 7. Chi-Square Value for MND Versus Other Decedents by Province over 21 Years

Province of Residence	Chi Square Value	Df	Significance Two- Sided
Prince Edward Island	22.978	20	0.290
Nova Scotia	28.513	20	0.098
New Brunswick	28.038	20	0.109
Quebec	85.987	20	0.000
Ontario	51.670	20	0.000
Manitoba	18.144	20	0.578
Saskatchewan	15.535	20	0.745
Alberta	36.687	20	0.013
British Columbia	18.122	20	0.579
Yukon	13.281	20	0.865
Northwest Territories	25.345	20	0.189
Newfoundland	18.761	20	0.537

Question Seven

What trends in hospital or non-hospital location of death for MND decedents in Canada can be identified for the years 1979 through 1999?

Over all years combined, 74.1% of all persons who were recorded as having died of MND died in hospital and 25.9% died in all other locations combined (see Table 8).

A significant difference over time in the hospital versus non-hospital location of death of MND decedents was found using chi-square analysis ($x^2 = 310.599$, df =

20, p = 0.000). A decrease in hospital-based deaths among the persons who died of MND was identified over these 21 years. In first year (1979), 81.6% of MND decedents died in hospital as compared 66.7% in the last year (1999).

Table 8. MND Decedent Location of Death Trends: 1979-1999

Year	Location of Death		Total
	Hospital N (%)	All Other N (%)	
1979	244 (81.6)	55 (18.4)	299 (100)
1980	264 (83.5)	52 (16.5)	316 (100)
1981	252 (82.1)	55 (17.9)	307 (100)
1982	272 (86.9)	41 (13.1)	313 (100)
1983	278 (79.0)	74 (21.0)	352 (100)
1984	296 (81.3)	68 (18.7)	364 (100)
1985	291 (78.6)	79 (21.4)	370 (100)
1986	302 (77.0)	90 (23.0)	392 (100)
1987	337 (79.9)	85 (20.1)	422 (100)
1988	244 (60.1)	162 (39.9)	406 (100)
1989	246 (56.0)	193 (44.0)	439 (100)
1990	321 (81.1)	75 (18.9)	396 (100)
1991	327 (76.2)	102 (23.8)	429 (100)
1992	382 (79.4)	99 (20.6)	481 (100)
1993	396 (75.0)	132 (25.0)	528 (100)
1994	404 (79.4)	105 (20.6)	509 (100)
1995	392 (72.5)	149 (27.5)	541 (100)
1996	399 (70.7)	165 (29.3)	564 (100)
1997	326 (60. 5)	213 (39.5)	539 (100)
1998	364 (68.0)	171 (32.0)	535 (100)
1999	351 (66.7)	175 (33.3)	526 (100)
Total	6,688 (74.1)	2,340 (25.9)	9,028 (100)

Significant Value: $x^2 = 310.599$, df = 20, p = 0.000

Conclusion

In summary, the data analysis revealed MND is a rare cause of death in Canada, although there has been an increase in the number of reported cases over time in keeping with an increase in total decedents each year. This proportional increase in MND deaths exceeded the increase in all other causes of death. Among the 9,028 people who were recorded as having died of MND, a slight but

significant increase in average annual age was noted from 1979 through 1999. Also, in 16 of the 21 years, more than half of all persons who died of MND were male. In five relatively recent years, however, more than 50% of the cases each year were female. This finding and others illustrate a slight increase in female cases. Among all MND decedents, a larger proportion were born in Canada than outside Canada each year and more were married than not married. In Quebec, Ontario, and Alberta, an increase in cases of MND versus all other cause of death cases was found over time. However, in the nine other provinces and territories, no change over time in cases of MND versus all other cause of death cases was found. A significant decrease in hospital-based deaths among persons who died of MND was also identified over these 21 years. A discussion of these findings in relation to the findings of past investigations follows in Chapter Five.

CHAPTER FIVE

Discussion of Findings

Information gained through this thesis study supplements the limited body of knowledge regarding MND in Canada and internationally. Given the minimal number of Canadian studies, it primarily advances an understanding of how this disease affects Canadians. In doing so, individuals with MND, their formal and informal caregivers, and the Canadian public are likely to benefit from this thesis study. This chapter compares and contrasts the findings of this research study with the findings of previous Canadian and international research investigations, and with additional published viewpoints. In keeping with the thesis research questions, this chapter is divided into sections focusing on: (a) prevalence rate and province of residence, (b) age, (c) marital status, (d) birthplace, (e) gender, and (f) location of death. The prevalence rate and province of residence sections are combined as they both illustrate the uncommon nature of MND. A discussion regarding the implications of these research findings for practice, policy, and health services follows each section.

Discussion of MND Prevalence and Province Residence Research Findings

This study revealed MND is a rare cause of death, although the prevalence rate of MND established in this study is higher than previous reported prevalence rates of MND. The gross mortality rate of MND established in this thesis study using 1979–99 Statistics Canada mortality data was 224.02 per 100,000 population. This is the highest reported prevalence rate of MND in both the Canadian and international literature. Among previous Canadian MND research literature, one of

the highest prevalence rates of MND was reported in an Alberta study. Svenson et al.'s (1999) study revealed the prevalence rate of MND for Alberta on July 1, 1995 was 6.07 per 100,000 population. A large discrepancy between the two studies is thus evident. This discrepancy in prevalence rates may be the result of research methods. This thesis study included the entire population who died of MND and other diseases in Canada from 1979 through 1999. Specifically, the 9,028 persons who were recorded as having died of MND in Canada during this 21-year period were included in this thesis study. In contrast, Svenson et al.'s study focused on one province and it included 171 individuals who had been diagnosed with MND in one year among the entire population of live Albertans. This thesis study involved the entire population who were recorded as having died of MND in Canada over a period of 21 years. By using data obtained on an entire population, although this population was entirely deceased, the prevalence rate of MND reported in this thesis study could be viewed as a more accurate reflection of MND in Canada. One drawback, however, is that prevalence rates are normally comprised of both live and deceased cases annually. This thesis study did not include live cases of MND, therefore MND cases in Canada are underreported, while the prevalence is over represented as MND decedent cases are not calculated against the entire live population. As mentioned, this thesis study investigated the prevalence rate of MND among individuals who died of MND. It does not include the prevalence rate of individuals who were still living with MND. As such, the research findings from this thesis study will be different than Svenson et al.'s study, as different populations were researched.

Another important distinction between Svenson et al.'s (1999) study and this thesis study is different time periods over which each respective prevalence rate was calculated. As, Svenson et al.'s study reported a prevalence rate on one specific day, July 01, 1995. This thesis study established a prevalence rate of MND in mortality data over a 21-year period. The research findings can be expected to be different, as the time period over which these prevalence rates were calculated varied.

Along with researching the overall mortality prevalence rate of MND over a 21-year period, this thesis study investigated changes in the prevalence rate of MND in Canada, and for each province and territory over time. A slight increase in the pan-Canadian prevalence rate of MND was found over time. In the first year (1979), the prevalence rate was 178.54 per 100,000 population. In 1999, the prevalence rate of MND had increased to 239.99 per 100,000 population. This increase corresponds with an increase in the number of MND cases reported each year, a growing number that exceeded the growth in total decedents each year in Canada. The least number of annual reported cases of MND was 299 in 1979 or the first year. A general increase each year was then noticed in the number of reported cases, with 526 persons or nearly twice as many persons reported as having died of MND in 1999. A proportional increase over time was also found for three specific provinces: Quebec, Ontario, and Alberta. In these provinces, a significant change (increase) over time, in the proportion of cases of MND as compared to all other causes of death combined was found using chi-square analysis.

One other Canadian study also investigated MND cases over time. Murray et al. (1987) found, for Nova Scotia, an increase in the incidence rate of ALS in the period of 1974 to 1979. More specifically, the incidence rate of ALS in Nova Scotia was 1.50 per 100,000 population for the period of 1974-79. The incidence rate of ALS nearly doubled in the next five years, as the incidence rate of ALS was established at 2.50 per 100,000 population in 1979-84. This increase is important to note, although Murray et al.'s study investigated incidence rates and this thesis study investigated prevalence rates, both found an increase in MND over time.

Similarly, among the international studies, an increase in incidence rates of MND was found in Scotland (The Scottish Motor Neuron Research Group, 1992). In contrast, four studies in Guam illustrated a decreased incidence and prevalence rate of MND from 1950 through 1994 (Garruto, Yanagihara & Gajdusek, 1985; Plato et al., 1986; Plato et al., 2003; Waring et al., 2004). Thus, the collective findings from these Guam studies are not consistent with the findings reported in this thesis study. However, as discussed in Chapter One, the people of Guam had an unusually high incidence and prevalence rate of MND, one that declined with dietary and perhaps other changes. Researchers in West New Guinea have also reported a decrease in both the incidence and prevalence rates of MND (Spencer, Palmer & Ludolph, 2005). As such, this study reveals MND is a rare disorder causing death, but one appears to be that is increasing in Canada while decreasing in other countries.

In summary, the prevalence rate of MND reported in this thesis study is the highest among the Canadian and international literature. Discrepancies in

prevalence rates of MND may be the result of the research method chosen for this thesis study, as it involved the entire population who died of MND from 1979 through 1999 as compared to all decedents in these years. As a result, it provides an accurate reflection of the mortality rate of MND in Canada. The thesis study also established that the mortality rate of MND increased over time. A study in Nova Scotia reported similar findings (Murray et al., 1987). Further research investigating the prevalence rate of MND in Canada since 1999 is now required, particularly if data on live cases can be incorporated, to continue to track MND in Canada.

Implication of MND Province of Residence and MND Prevalence Research Findings

The implications of the following findings on province of residence and prevalence rate for MND are primarily based on the rarity of MND. Few individuals appear to be suffering from and dying of MND. The rare nature of MND may be the result of a general lack of awareness among medical professionals regarding testing for MND or inadequate diagnostic tests. Some individuals who have a MND may not be diagnosed as a result. MND disease symptoms may also be missed as they may be confused with those of other diseases and of the aging process itself (Leone, Chandra & Schoenberg, 1987). Individuals with MND may also minimize or deny their symptoms, causing a delay in diagnosis or no diagnosis. An increased awareness among all health care professionals and the general public is necessary in order for this disease to be better understood and accurately diagnosed. A lack of knowledge regarding MND

among health care professionals has already been identified by individuals with MND (Hughes, Sinha, Higginson, Down & Leigh, 2005). Health care professionals have also identified a need for their own increased knowledge about MND (Mitsumoto et al., 2005). It stands to reason that educational in-services regarding MND for health professionals and the general public are critical so those affected by MND can receive an accurate diagnosis and thus proper ongoing care or support.

Although MND is rare, the findings of this thesis study revealed MND is becoming more common over time. Further research is required to determine whether MND has continued to become more common since 1999. With increased awareness among health care professionals and the general public, more individuals may be diagnosed with MND, increasing the prevalence rate of this disease and also perhaps spurring better diagnostic tests, treatments, and supportive programs or services for these people and their families.

Discussion of MND Age-based Research Findings

This thesis study found the mean age at death from MND has increased over time. More specifically, among the 9,028 people who were recorded as having died of MND, a slight but significant increase in average age was noted from 1979 through 1999. This significant difference was found using ANOVA, which compares the mean age each year of persons who died of MND. The Pearson one-tailed correlation test also revealed a significant positive correlation (although weak), as calculated on the basis of age at death and year of death. These tests both demonstrate that people are either living longer with MND or are not encountering

a MND until later in life. In 1979, the mean age at death was 61.7 years, while in 1999, the mean age at death was 65.8 years; a considerable increase of 4.1 years in only 21 years.

In contrast, Mandler et al.'s (2001) study of Canadians and Americans found the mean age at death from ALS was 62.0 years in the years 1997-2001, while two earlier studies reported an older mean age at death. Svenson et al. (1999) found the mean age at death in Alberta from MND was 66.2 years for the 1994-95 year. Researchers in Ontario similarly reported the mean age at death from ALS in 1978-82 was 65.9 years for males and 68.0 years for females (Hudson et al., 1986). These three studies indicate that life expectancy with MND has decreased in recent decades, in stark contrast to the findings of this thesis study.

The discrepancy, therefore, is based on whether or not the mean age at death from MND has increased or decreased. This thesis study established the mean age at death from MND as increasing while a comparison of previous Canadian literature indicates the mean age at death from MND has declined. This discrepancy may be the result of different research methods. As mentioned, Mandler et al.'s (2001) recent study reported the youngest mean age at death. In Mandler et al.'s study, a one-page form with 11 questions was used to gather data. Age at death was not listed as a question on this form. Therefore, it remains unknown how this information was obtained. Also, the number of Canadians in Mandler et al.'s sample was not reported, and Canadians findings were not reported separately from the American findings. The findings in this study are less reflective of Canada, as ALS may affect Canadians differently than Americans.

Despite this discrepancy, similarities among this thesis study and previous research are apparent. The mean age at death from MND (66.2 years in 1994-1995) that was reported in Svenson et al.'s (1999) study is similar to the mean age at death in 1999 (65.79) reported in this thesis study (65.79 years). This is a difference of only 0.41 years. Similarities in the mean age at death from MND are also evident when the international findings and the findings of this thesis study are compared. In Okamoto et al.'s (2005) Japanese study, the mean age at death in 2001 from ALS was 67.8 years. As previously discussed, the mean age at death for MND decedents in 1999 established by this thesis study was 65.79 years. A difference of 2.01 years is thus evident. In addition, a difference of 2.5 years is present when this study and Mandrioli, Faglioni, Merelli, and Sola's (2003) study are compared, as those researchers reported a mean age at death as 68.29 years in Modena, Italy for the years 1990-99.

In summary, this thesis study established that the mean age at death from MND has increased over time in Canada. Previous Canadian research collectively suggested that the mean age at death from MND is declining. This discrepancy may be the result of research methods, with this thesis study based on Canadian population-level mortality data over a 21-year period. Along with discrepancies, similarities have also been noted among the Canadian and international research investigating the mean age at death from MND, an age which is a premature death, but with death occurring most often at or near the age retirement.

Implication of MND Age-Based Research Findings

As discussed previously, this thesis study found that the mean age at death from MND has increased over time. Deaths from MND unaccountably ranged from 0 years of age to 100 years of age, with the mean age at death being 64.3 years over the entire 21-year study period. Since there is no cure for MND, an increased life expectancy may reflect improvements in life support or health care technologies such as antibiotics, mechanical ventilator support, and gastrointestinal tube feedings. Individuals with MND eventually become completely disabled, with invasive ventilation and gastrointestinal tube feeds needed to sustain life (Lyall, Donaldson, Polkey, Leigh & Moxham, 2001). Individuals with MND may choose to extend their life by these artificial means and thus increase their life expectancy. The increased life expectancy of individuals with MND may therefore be at a great economic cost. Prolonging life through artificial support in a debilitated state also raises difficult ethical questions regarding the quality of this life (Smyth, Riedl, Kimura, Olick & Siegler, 1997). Little is known regarding the quality of life among individuals with MND who are using artificial means to live. Understanding the nature of artificial life support inventions such as invasive ventilation and gastrointestinal tube feeding provides insight into the quality of life for those receiving this support.

Invasive ventilation provides mechanical ventilation through an endotracheal tube or a tracheostomy tube. An endotracheal tube passes through the month or nose into the trachea (Mechanical Ventilation, 2006). Similarly, a tracheostomy tube is inserted through the neck into the trachea (Mechanical

Ventilation). Individuals receiving this form of life support cannot verbally communicate with their family or others. In order to remain alive, however, they will require continuous invasive ventilation once intubated, as respiratory failure is the principle cause of death for individuals with MND (Lyall, Donaldson, Polkey, Leigh & Moxham, 2001; Walling, 1999). A gastrointestinal feeding tube or G-tube is a tube inserted through a small incision in the abdomen into the stomach to provide long-term liquid nutrition (Feeding Tube, 2006). Individuals with MND who receive this support cannot feed themselves or swallow, and so will require specialized daily gastrointestinal tube feeding and care. As they eventually become more disabled, individuals with MND cannot complete other basic activities of daily living and thus cannot care for themselves (Thompson & Swash, 2001). The quality of life of individuals with MND receiving these forms of artificial life support may therefore be significantly jeopardized.

Their dignity may also be affected, as individuals with MND eventually become dependent on others for their basic care. Sue Rodriguez, a Canadian woman diagnosed with ALS, attempted to avoid this by fighting for the right to physician-assisted suicide (Kluge, 1993). It was argued that the criminal code violated the ethical principle of beneficence, as her dignity was violated by the progressive nature of ALS (Kluge). For many individuals with MND, artificial life support could be viewed as causing the individual with MND further suffering, as physical decline will be prolonged and emotional harm may result from these interventions. Families could also experience undue suffering as life support prolongs the debilitated state of their loved one and thus can prolong their grieving

process. While life can be extended, the question is whether the individual, their family, and the larger society have benefited.

Providing artificial life support when there is no chance of recovery also ignores the underlying issue that individuals with MND face - their impending death. Health care professionals are often not comfortable in raising end-of-life decision issues (Mitsumoto et al., 2005). Consequently, discussions regarding end-of-life care planning may not take place, with appropriate palliative care delayed (Mitsumoto et al.). Health care professionals often prefer to sustain a life rather than support a death.

Sustaining life through artificial support has other ethical and practical implications. The high cost of life support for an individual with MND may not be ethically justified when there are other areas of the health care system that do not receive adequate financial support (Russell, 1998). For instance, palliative care services in Canada may not receive adequate funding. Although Health Canada currently has a national strategy for palliative and end-of-life care through the Secretariat on Palliative and End-of-Life Care, palliative care is currently under-funded and also vulnerable to funding cut-backs (Quality End-of-Life Care Coalition of Canada, 2005). The federal government recently reduced funding to the Secretariat on Palliative and End-of-Life Care, from 1.7 million in 2005-06 to $470,000 (with $300,000 funding still pending) in 2006-07 (Canadian Hospice Palliative Association, 2006). Palliative and end-of-life care was also reduced in the 1990's when health care restructuring took place, as institutional palliative care beds were reduced in number across Canada (Carstairs & Beaudoin, 2000). In

addition, few provinces have a designated budget for palliative care (Carstairs & Beaudoin). It is therefore not surprising that palliative care services largely depend on charitable donations (Carstairs & Beaudoin). Additional funding for palliative and end-of-life care is required in order to meet the demands of all dying Canadians, particularly as the number of deaths in Canada is expected to increase by 33% by the year 2020 and more as the baby boom generation moves through retirement (Quality End-of-Life Care Coalition of Canada, 2005).

Increased funding for palliative care is particularly important for individuals with MND. A recent study found palliative care, preparation for death, and avoiding the prolongation of dying were some of the needs identified by individuals with ALS (Ganzini et al., 2002). Funding for palliative care should be a priority. Similarly, health care professionals need to address end-of-life issues with MND victims. This includes discussions regarding advanced directives. The issue of advanced directives is a delicate, yet necessary, matter. Advanced directives provide individuals with a method to identify their health care preferences for the event that they become incompetent to make such decisions (Advanced Directives, 2006). Specifically, instructional advanced directives, also called living wills, allow an individual to identify what or how health care decisions are to be made if they become incompetent (Advanced Directives, 2006). Health care professionals can assist by providing information regarding the disease progression, decisions to be addressed including mechanical ventilation, and other care needs (Young et al., 1994). Providing information regarding disease pattern, progression, and outcome is necessary in order for individuals with MND to make informed end-of life

decisions and prepare for impending health problems. Determining the amount of information to provide is critical. Health care professionals may provide too much information to individuals with MND. This is known as truth dumping, where the ill individual is left feeling hopeless (Muskin, 1998). It is necessary that health care professionals find a balance between not informing patients regarding their illness and treatment options versus providing too much information about MND, causing a sense of despair in the ill individual (Muskin).

Determining when to discuss advanced directives is also critical. There is limited knowledge regarding when the topic of advanced directives should be addressed. As mentioned in Chapter One, individuals with MND typically develop slurred and nasal speech, making communication difficult (Mayeux, 2003). Persons with MND normally do not live as long as other persons. Thus, addressing the issue of advanced directives in a timely manner is particularly important for MND victims. Delaying these discussions may have significant consequences including incomplete or absent personal directives resulting in an undue emotional decisional burden on family, friends, and health care professionals. Further research investigating when to discuss advanced directives and how much information to provide is necessary in order for MND victims to make informed end-of-life decisions.

Along with providing information, health care professionals can assist with advanced directives in other ways. The role of health care professionals may involve facilitating a dialogue with family, as family members provide a unique and invaluable source of support. As advanced directive decisions are considered

more personal than medical, the family may have an important role in advanced directive decisions (Young et al., 1994). They may also have a critical role in ensuring their ill loved one's advanced directives are actually carried out (Young et al.). Health care professionals can support individuals with MND by involving other members of their support network. As advanced directive decisions may be more personal than medical, further research regarding the role of health professionals in assisting individuals with MND make difficult decisions is required.

As mentioned, this thesis study established that the mean age at death from MND is increasing over time, with the mean age at death being 65.8 years, in 1999. The older mean age at death from MND found in this thesis study may be the result of an improved level of general health among the population. Consequently, individuals with MND are living longer. Other reasons for an increased mean age at death among MND decedents may be the result of delayed onset or a prolonged duration of MND. However, further research investigating this is required.

Research investigating a cure for MND is also important. Although the mean age at death from MND is increasing over time, individuals with MND, die prematurely. In 1996, the life expectancy in Canada is 78.6 years (Beaudet et al., 2000), with minimal but certain increase to 1999. As there is no cure for MND, further research investigating possible cures for this disease is necessary, such as "gene" therapy and pharmaceutical research. Pharmaceutical research in particular is an important area for future studies, as this research may establish a cure for MND. Pharmaceutical research may also advance the limited drug treatments

available to individuals with MND. As discussed in Chapter One, the drug Riluzole is used for MND, as it slows the deterioration in muscle strength and increases survival by 3 to 6 months (Grovenveld et al., 2003; Thompson & Swash, 2001). Additional pharmaceutical research could improve the quality of life for individuals with MND by establishing a cure or expanding drug treatments for MND. Other treatments for MND are limited to palliative care and involve the management of MND symptoms (Grovenveld et al., 2003; Thompson & Swash, 2001).

Other important areas for further research include epidemiological research. As discussed in Chapter One, several causative theories have been proposed. Although the biological or other processes that contribute to the development of MND are not fully understood, these theories provide foundational knowledge for further epidemiological MND research. In addition, these theories identify risk factors for MND, and identify behaviors that may prevent the development of this disease. Behaviors that prevent MND are particularly valuable for those individuals who have a familial history of MND. As discussed, cycad seeds found in the West Pacific have been associated with the development of ALS in the Chamorros population (Steele & Guzman, 1987). Other foods that should be consumed cautiously include foods containing glutamate such cheese, milk, tomato juice, mushrooms, and fish (Problem Additives, 2002, p.1). These food products are thought to increase the risk of developing MND. Individuals with a diet high in glutamate have a more than three times higher risk for developing ALS as compared to those with a diet low in glutamate (Neilson, Matkin, Longstreth & McGuire, 2000). As such, avoiding cycad seeds and reducing consumptions of

foods containing glutamate may prevents the development of this disease.

Other health promotion behaviors include the cessation of smoking. It is well known that smoking is an unhealthy behavior contributing to the development of several different diseases. One of these diseases is MND, as smoking causes oxidation damage and thereby increases the risk of MND by 70% (Kamel et al., 1999). Health care professionals need to educate their patients regarding these preventative behaviors to reduce their risk of developing MND. In particular, health professionals need to educate those individuals with a family history of MND, as they have a greater risk for developing this disease (Rowland & Shneider, 2001). Further epidemiological MND research is required and may establish more conclusively the cause of this disease. In doing so, it will provide the public with additional knowledge to prevent the development of new cases of MND.

In summary, the increased life expectancy of individuals with MND established in this thesis study may be simply the result of advances in health care technology, such as artificial life support. Artificial life support interventions may prolong life but not improve the quality of this life. Ethical and practical implications result from these interventions. The ethical principle of beneficence comes into focus as a result of these interventions. The issue of appropriate allocation of health care funding also arises from these interventions, particularly as palliative care services do not appear to receive adequate funding (Wilson, 2002). Increased funding for palliative care and other changes in the health care system is necessary in order for those individuals dying of MND to receive quality palliative and end-of-life care. Further research regarding the role of health care professionals

in assisting individuals with completing advanced directives is also necessary. Additional pharmaceutical, gene and epidemiological research is also important, as this research may establish better treatments as well as the cause of and a cure for MND.

Discussion of MND Marital Status Research Findings

As revealed in Chapter Four, this thesis study found 63.2% of MND decedents were married and 36.8% were not married (over all 21 years combined). The national research on marriage suggests similar findings. In 1996, 75.3% of Canadians were married, which is a decline from 78.7% in 1986 (Statistics Canada, 1999). This thesis study established in each year from 1979 through 1999, over 58% of MND decedents were identified as married at the time of their passing. These findings are consistent with those of two previous research studies (Gross-Paju et al., 1998; Mandler et al., 2001). Mandler et al.'s study primarily investigated end-of-life patterns of care and therapy for ALS patients in Canada and the United States by examining data from an ALS patient care database. Although marital status was not the focus of the study, information was collected on this variable. Mandler et al. found 78.1% of the individuals with ALS in this database were married, with their spouse the primary caregiver in most cases. It was not reported whether the remaining 21.9% of individuals with ALS in this database were single, divorced, or widowed. Similar findings were reported in Gross-Paju et al.'s South Estonia study. This study focused in part on whether individuals were living with their spouse or living alone when diagnosed with ALS. Among all 108 subjects, 57.4% were living with their spouse at the time of diagnosis. These

researchers also reported more males than females were living with a spouse at the time of their diagnosis. Specifically, 75.9% of males and 37.5% of females were living with a spouse at the time of their diagnosis.

These findings indicate that individuals with MND are more often married then unmarried and also that they have remained married despite the challenges of this disease. Mandler et al.(2001) and Gross-Paju et al. (1998) reported that most individuals diagnosed with ALS were either married or living with a spouse. A past study of individuals with MND and other neurodegenerative diseases revealed they identified their spouses as the most important person to them (Aoun, Kristjanson & Oldham, 2006). Furthermore, another study showed not only are spouses the most likely to provide emotional support, but they are also the most likely to provide direct care to their ill partner (Chipchase & Lincoln, 2001).

Implications of MND Marital Status Research Findings

As mentioned, this thesis study established more individuals with MND are married than not married at the time of their death. This situation has implications regarding caregiver burden, as spouses often assume the role of caregiver when one of the partners in a marriage becomes disabled or chronically ill (Chipchase & Lincoln, 2001). It is likely that spousal caregivers of individuals with MND are in mid-to-old age, since this thesis study established the mean age at death from MND was 65.8 years in 1999 or 64.3 years over all years combined. Older caregivers can experience additional physical strain, as they more often have physical limitations than younger caregivers. By 65 years of age, 77% of Canadian men and 85% of Canadian women have at least one chronic condition (Gilmour &

Park, 2003). Outcomes of physical strain faced by spousal caregivers and other informal caregivers include depression, low self-reported health, and poor health maintenance or promotional behaviors (Burton, Zdaniuk, Schultz, Jackson & Hirsch, 2003). Some caregivers have also reported problems with everyday memory, and additional overall physical complaints (Chipchase & Lincoln). In general, health outcomes associated with long-term caregiving have a downward trajectory (Burton et al.). Many family caregivers are overwhelmed by feelings of never-ending work and responsibilities (Corbin & Strass, 1988).

Along with physical strain, caregivers often experience emotional strain as they watch their loved one change from their former self (Chipchase & Lincoln, 2001). Leisure time away for caregiving is difficult to plan when there is an ill or disabled partner (Boeij, Duijnstee & Grypdonck, 2003). Caregivers and partners often become confined to their home (Boeij et al.). Other sources of emotional strain for family caregivers include concerns for the health of their partner and their own capacity to provide care (Cheung & Hocking, 2002). Caregivers may also worry about financial matters, as many affected families experience financial difficulties (Chipchase & Lincoln; Chochinov & Kristjanson, 1998). Financial difficulties arise as the ill spouse is unable to work and many caregivers reduce their employment outside the home to care for their ill partner, resulting in a loss of income (Boeij et al.). Despite these challenges, many caregivers continue to provide care. Caregivers may draw their strength from the person receiving care (Strang & Koop, 2003). Others view their caregiving with pride, and recognize it as a gift that they are glad to give to their loved one (Koop & Strang, 2003). Spousal

caregivers may be motivated by conjugal ethics, in keeping with their marriage vows and the promise to take care of each other until death (Boeije et al., 2003). This ethic, possibly combined with a loving relationship, contributes to the caregiver maintaining the caregiving role (Boeije et al.). Another possible reason that spouses continue to provide care is the belief that no one is to blame for this misfortune of ill health (Boeije et al.). Spouses may provide care as they would want their partner to demonstrate the same willingness to be caregivers if circumstances were reversed (Boeije et al.). Caregivers may also not feel they have a choice, as there is no one else available to provide care (Boeije et al.). Other informal caregivers such as children and friends are commonly involved in caregiving, although they do not replace a spouse when there is one.

Regardless of the reasons, spousal caregivers and other informal caregivers offer an invaluable service to the ill individual and society. Their contribution is significant, and is of substantial economic value to society (Wilson et al., 2005). In fact, if caregivers stopped providing care, the health care system would be overwhelmed (Armstrong & O'Grady, 2004). Despite this, informal caregivers receive little recognition and support for their work. Few policies have been established that support caregivers, indicating their contributions remain largely invisible to administrators and policy makers. However, in 2004, the federal government passed the *Compassionate Care Benefit*. Unfortunately, it falls short in recognizing the contributions of informal caregivers. Only those employed caregivers who have accumulated 600 insured hours can receive compassionate care benefits and they only receive up to 55% of their average insured earnings for

a maximum period of six weeks (Armstrong & O'Grady). Many informal caregivers remain ineligible for benefits. Seniors, stay-at-home parents, the self-employed, and employees who do not have 600 insured hours are not eligible for compassionate care benefits (Armstrong & O'Grady). Even those individuals who are eligible for compassionate care benefits receive only half of their normal income. The marital status findings of this study suggests the *Compassionate Care Act* should be expanded so that informal caregivers receive full financial compensation and the Act expanded to include seniors, stay-at-home parents, the self-employed, and individuals who work part-time. Klie (2006) also believes that the paid leave-of-absence period should be increased from six weeks and the definition of family expanded.

Along with financial support, informal caregivers require emotional support. As mentioned previously, many are emotionally strained from the burden of caregiving. Formal supports may be needed, so caregivers can express their thoughts and feelings regarding caregiver issues, as emotional support services have been found important for caregiver satisfaction (Savard et al., 2006). The ALS Society of Canada offers support to individuals with ALS and their families through ten provincial ALS Societies. This support includes information, referral, equipment loan, and advocacy (ALS Society, 2006). A support program for caregivers of individuals with MND has not been implemented. This may be one of the reasons why only 37% of individuals with ALS and their families reported satisfactory support from the ALS Society of Canada (Martin & Turnbull, 2001).

Formal home care programs also appear to offer limited emotional support to caregivers. Home care support normally includes physical care of the individuals with MND, such as bathing and wound care. Respite care may also be offered to allow caregivers a physical break in care, thus enabling them time away to go shopping or engage in other activities outside the home. However, time away from caregiving may not provide emotional support to caregivers or an adequate break. Caregivers describe respite in terms of a mental state where there is freedom from worry and responsibility of caregiving (Strang, Koop & Peden, 2002). A local study found that when respite involved being physically separated from the caregiving environment, this feeling of freedom from caregiving was not achieved (Strang et al.). Program planners for home care need to utilize research-based evidence when creating respite programs. Limited home care funding is another issue. Home care programs should be expanded to meet not only the physical needs of the client but also the emotional needs of the caregiver.

Currently, eligibility requirements for most home care programs are based on the ill individual's assessed needs for support rather than the caregiver's needs. Even though home care programs depend on the care given by friends and family, as care is rarely provided 24 hours a day. In short, informal caregiving is a requirement of home care programs for dependent persons. Otherwise, institutional care is needed. One of the most significant problems with home care is the limited number of hours for which nursing care and homemaker support is available (Carstairs & Beaudoin, 2000). This policy is reflected in the needs assessment in home care as well. The needs assessment considers care given by spouse or other

family member (Boeij et al., 2003). In some cases, spouses or other family members are expected to provide 24-hour care (Cheung & Hocking, 2004). Overall, home care services are inadequate and limited (Bruera, Kueh, Emery, MacMillian & Hanson, 1990; Thorpe, 1993). A recent study reported home care services are provided, over an increasingly shorter period of time (Wilson et al., 2005). The burden of care has been transferred to the family (Carstairs & Beaudoin). In addition, many individuals and families do not receive any home care. When individuals and families do not request home care support, referrals to home care are frequently neglected.

Family caregivers, particularly older spouses, may have a limited ability to provide care as a result of old age, health problems of their own, or caregiver strain from long-term and daily caregiving. Although most family caregivers may be able to provide care in the short term, they may lack ability to provide care in the long-term. Caregiver strain may also occur when there is more than one family caregiver. One study found a care network consisting of mainly elderly caregivers was less able to meet the demands of long-term caregiving, as the caregivers themselves become frail (Fast, Keating, Otfinowski & Derksen, 2003). These finding indicate that home care services need to depend less on informal caregivers with additional nursing care and homemaking hours provided to stop hospitalizations and institutionalizations of the ill person, and the impact of strain for family caregivers.

Further research on home care is also required so that the needs of caregivers are better understood. The proposed national strategy on palliative and

end-of-life care suggests further research should focus on the needs of families and informal caregivers (Quality End-of-Life Care Coalition of Canada, 2005). This work should be supported by further funding of this area of research, such as through Health Canada or other funding sources such as the Canadian Institute of Health Research.

Another issue is that there are other burdens the family and individuals assume, including the costs of drugs and equipment such as pain pumps, oxogen, and commodes (Carstairs & Beaudoin). Home care expansion needs to include, beyond more nursing care and homemaker, financial coverage for drugs, equipment, professional, and non-professional care services. In addition, 24-hour pain and symptom management is a necessity for home-based care (Carstairs & Beaudoin, 2000).

Expanding home care services may not be enough to provide adequate support to individuals with MND and their caregivers. In a recent study, a need for ongoing information and support was expressed by 68% of individuals with ALS and their families (Martin & Turnbull, 2001). Other researchers have similarly reported that caregivers value information and advice (Savard et al., 2006). Health care professionals should be aware of the need for ongoing information and provide this support on an ongoing basis. Discussions regarding the needs of individuals with MND and their families are important in order to identify other unmet needs and thus provide adequate support. These discussions should be ongoing, as needs change over time. As mentioned previously, only 37% of individuals with ALS and their families have reported satisfactory support from the ALS Society of Canada

(Martin & Turbull). Additional research investigating the needs of individuals with MND and their families is important. This research may subsequently inform and change the services provided by the ALS Society of Canada.

In summary, spouses and other informal caregivers make a significant care contribution, which relieves the health care system and society of much of the costs associated with care for ill and dependent MND victims. Despite this, they receive little support or financial compensation. Consequently, many experience caregiver burden, with physical, emotional, and financial strain. Respite services offered through home care programs appear to provide little relief or emotional support for the caregiving role. Provincial home care programs are limited in the amount professional and non-professional services offered; and many do not include the cost of drugs, supplies, and equipment. A comprehensive home care program is required in which the burden of care is more evenly shared with the health care system, rather than individuals and families solely or primarily. In addition, the *Compassionate Care Benefit* should be expanded to increase the number of caregivers eligible for it, increase the length of time caregivers can receive income support, and raise the income replacement. Further research investigating the unknown and unmet needs of caregivers is required, so that policies and programs reflect these needs.

Discussion and Implication of MND Birthplace Research Findings

Among all 142 studies reviewed, none investigated the incidence, prevalence, or mortality rates of MND on the basis of birthplace. This thesis study revealed a significant difference over time in Canadian versus non-Canadian

birthplace among MND decedents, with a small decline in the percentage of MND decedents born in Canada over the 21-year period. In the first study year (1979), 76.6% of MND decedents were born in Canada as compared to 75.0% in the last study year (1999). Over all years combined, 76.3% of MND decedents were born in Canada and 23.7% were born outside of Canada. These findings provide insight into the risk factors associated with MND, as most individuals who die of MND in Canada were born in Canada and presumably lived most, if not all, of their lives in Canada. Early environmental risk exposures, food sources, and other influences native to Canada may thus predispose a person to this disease, and be responsible in full or in part for the development of MND later in life. Further research that includes the birthplace of live MND victims and decedents is required, as this research has etiological importance. Epidemiological research provides insight into whether MND is unique or common to a population. In doing so, birthplace research provides clues into whether MND is more prevalent among a specific ethnicity group or geographical area, and thus may pinpoint genetic, environmental, or other influences triggering or causing MND.

Discussion of MND Gender-Based Research Findings

Gender-based MND rates have been researched in three previous Canadian studies and several international studies. The three previous Canadian studies all found the incidence, prevalence, or mortality rates of MND were higher among males than females (Hudson et al., 1986; Murray et al., 1987; Svenson et al., 1999). Similar findings were reported among the international studies, as most reported males have a higher predominance of MND as compared to females (Alcaz et al.,

1996; Annergers, Appel, Lee & Perkins, 1991; Bettoni et al., 1994; Briani et al., 1996; Chazot, Vallat, Hugon, Lubeau & Dumas, 1986; Chazot, Vallat, Hugon, Lubeau & Dumas, 1987; Chio, Magnani & Schiffer, 1993; Domenico et al., 1988; Durrleman & Alperovitch. 1989; Elian & Dean, 1992; Forbes, Colville & Swingler; 2004; Forsgren, Almay, Holmgren & Wall, 1983; Fong et al., 1996; Fong et al., 2005; Giagheddu et al., 1983; Giagheddu et al., 1993; Govoni, Granieri, Capone, & Manconi & Casetta, 2003; Granieri et al., 1988; Gross-Paju, et al., 1998; Hojer-Pedersen, Christensen & Jensen, 1989; Huber & Henn, 1995; Kahana & Zilber, 1984; Kihira et al., 2005; Logroscino et al., 2005; Lopez-Vega, Calleja, Combarros, Polo & Berciano, 1988; Mandriolo, Faglioni, Merelli & Sola, 2003; McGuire, Longstreth, Koepsell & van Belle, 1996; Okamoto et al., 2005; Okumura, 2003; Piemonte et al., 2001; Plato et al., 2003; Riggs, 1990; Salemi et al., 1989; Seljeseth, Vollset & Tysnes, 2000; The Scottish Motor Neuron Research Group, 1992; Traynor et al., 1999; Tysnes, Vollset & Aaril, 1991; Veiga-Cabo, Almazan-Isla, SendraGutierrez & Pedro-Cuesta, 1997; Waring et al., 2004; Yoshidi et al., 1998). In contrast, this thesis study found that in four of five relatively recent years (1987, 1993, 1994, 1996, and 1997), more than 50% of MND decedents each year were female. Furthermore, there was a slight increase in female cases over time. In the first year (1979), the sex-based ratio was 1.3 males to 1.0 female and in the last year (1999) this ratio was 1.2 males to 1.0 female.

The sex-based discrepancy in findings between this thesis study and the previous research may be the result of underreporting of MND among women in previous years (Seljeseth, Vollset & Tysnes, 2000). The discrepancy could also be

due to research methods and/or improved case ascertainment. As discussed in Chapter Two, all past Canadian MND studies are one to two decades old. Many of the international studies are also dated. Research methods have developed over the years. Another issue with the past Canadian and international literature is that case ascertainment may not be high, since many studies involved a population subset or sample. However, this thesis study involved the entire population of people who died of MND and other causes in Canada from 1979-99. As such, a higher case ascertainment is expected, making the gender findings in this thesis study a potentially more accurate reflection of the sex-based prevalence of MND in Canada.

Implication of MND Gender-Based Research Findings

As discussed, this thesis study established there was an increase in female cases of MND over time and in five relatively recent years (1987, 1993, 1994, 1996 and 1997), more than 50% of MND cases each year were female. This trend has implications regarding the care of women suffering from MND, as women are most often the persons who become informal caregivers (Canadian Institute for Health Information, 2000, p. 60). Women typically shoulder a large portion of the care in the home and community (Carstairs & Beaudoin, 2000). One study found male-dominated networks provide fewer hours of care than networks dominated by women (Fast et al., 2003). Consequently, women are more likely than men to have unmet care needs (Wilkens & Park, 1998, p. 42). Women may therefore need to rely on other sources of care, such as friends or adult children. They may also depend more on formal care as compared to men (Grabbe et al., 1995). While

living in a private residence, women receive more formal care than men, as home care services are used more often by women than men (Senior's Health Care Use, 2003, p.2). Furthermore, if such support is lacking, women may need to move from a private residence into a nursing home, hospice, or hospital to receive care.

As discussed, women are typically the informal caregivers; providing care to their children, extended families, ill family members, and the larger community through volunteering and other work. Thus, when a woman develops MND the implications are significant. Women suffering from MND and their families are at greater risk of having unmet needs than men suffering from MND. Formal home care needs to be increased, allowing women with MND to remain as long as possible in their home. Formal sources of care are also required to ensure the caregiving responsibilities that women often have are met. In addition, policy changes need to occur so women are adequately compensated for their caregiving contribution. As mentioned in a previous section, the federal government passed the *Compassionate Care Act* in 2004, which partially compensates caregivers who have accumulated 600 insured hours. This is limited to 6 weeks of assisted leave. However, women are most likely to be ineligible for compassionate care benefits, as it is women who make up the majority of stay-at-home parents and it is women who most often work part-time, managing child rearing and other domestic responsibilities (Armstrong & O'Grady, 2004). Women provide more than 80% of the unpaid care for the elderly or the disabled and three out of four unpaid caregivers are women (Armstrong & O'Grady). As such, the *Compassionate Care Act* needs to be revised significantly to include those caregivers who are self-

employed and those caregivers who have part-time employment. Furthermore, the income support should increase from 55% to 80 or 100%, in keeping with most paid leave of absences.

Other apparently hidden costs in providing informal care include the high cost to the caregiver's health. As previously discussed, caregivers experience physical and emotional strain from providing ongoing informal care. As women provide the majority of informal caregiving, they are most likely to experience caregiver strain (Armstrong & O'Grady, 2004). Additional support programs should be established for women caregivers, offering them emotional support and counseling. A comprehensive home care program that addresses the largely gender-based issues involved in providing care are also required (Armstrong & O'Grady).

As discussed previously, this thesis study established an increase in female cases of MND over time. This finding is revealing about the cause of MND. As mentioned in Chapter One, certain occupations have high rates of MND, with work-based exposure to chemicals thought to be a risk factor for developing MND. Although these specific chemicals remain largely undetected, military personnel and agricultural workers have an increased risk for developing MND (McGuire, Longstreth, Nelson, Koepsell & Checkoway, 1997; Weisskopf et al., 2005). The increase in female cases of MND established in this thesis study may be the result of females increasingly holding positions that have more traditionally been held by men (Domenico et al., 1988; Granieri et al., 1988). This increase in female cases of MND over time, as established in this thesis study, deserves further epidemiological research.

An increase in female cases of MND over time has other implications regarding medical treatment, including diagnosis. Women may experience a delay in receiving a diagnosis of MND, as health professionals could be largely unaware that women have an increased prevalence of MND (Logroscino et al., 2005). Many individuals with MND have reported that health professionals lack knowledge or have an incomplete understanding of MND (Hughes et al., 2005). An increased awareness among health professionals is required so that women who have MND are cared for appropriately. An increased awareness of MND among health care professionals can be achieved by attending in-services and reading current research regarding MND. Women also need to be aware that more women are developing MND over time and should seek health care intervention as soon as symptoms occur. It is currently thought that women and men experience the same symptoms of MND. Further research among women is required to better understand whether this disease affects women differently.

In summary, this thesis study established that there was an increase in female cases of MND over time. As discussed, women are most often the caregivers to others. Female MND victims may require additional home care services, as they have fewer informal sources of care and more caregiving responsibilities. In addition, compassionate care benefits need to be expanded to include those caregivers who are self-employed and employed part-time. Such that, women may be more recognized and compensated for their caregiving contributions. The increase in female cases of MND, reported in this thesis study, may be the result of more females holding positions previously held by men. More

females may be exposed to occupational toxins responsible for the development of MND. Further epidemiological research is required to explain the increase in female cases of MND. It is also necessary for health professionals and the general public to have an increased awareness of the increased risk of MND among women.

Discussion of MND Location of Death Research Findings

Only one previous study among all of the Canadian and international literature investigated location of death for MND decedents. Mandler et al.'s (2001) study investigated end-of-life patterns of care and therapy for ALS patients in Canada and the United States by examining data in one ALS patient care database. Although location of death was not the focus of the study, information was collected on location of death from 1997 through 2001. Among the 1,014 Americans and Canadians with ALS; Mandler et al. found 64.1% died at home, 20.7% died in hospital, 7.7% died in nursing facility, and 6.9% died in a hospice. This thesis study found a considerably different location of death pattern than Mandler et al. Over all years combined, 74.1% of all Canadians who were recorded as having died of MND died in hospital and 25.9% died of MND in all other locations. Furthermore, a significant decrease in hospital-based deaths among persons who died of MND was identified over these 21 years. In first year (1979), 81.6% of MND decedents died in hospital as compared 66.7% in the last year (1999). Regardless, the majority of deaths continued to take place in hospitals.

A number of discrepancies between Mandler et al.'s (2001) study and this thesis study are relevant for discussion. Mandler et al. found more ALS decedents

died at home than in hospital while this thesis study established more MND decedents died in hospital than in all other locations combined. This discrepancy may be the result of Mandler et al.'s study methods. Mandler et al. did not report Americans findings separately from Canadian findings, such that the study may be less reflective of the Canadian situation, as American and Canadian health care systems are dramatically different. American seniors with Medicare Hospital Insurance benefits, who have been certified by a physician as terminally ill, with a life expectancy of six months, are eligible for Medicare Hospice Benefits (Medicare Hospice Benefits, 2005). Hospice benefits are based on home care support, including: Professional and non-professional services, short-term respite care, and medical supplies (Medicare Hospice Benefits). Certain drugs for symptom and pain management are also included, although with a co-payment (Medicare Hospice Benefits). Short-term in-patient care is also covered by the Medicare Hospice Benefit, although care is expected to occur in the home (Medicare Hospice Benefits). Consequently, more Americans with Medicare hospice benefits die at home as compared to Canadians who lack this level of support.

Implications of MND Location of Death Research Findings

As indicated, this thesis study found more individuals with MND die in hospital than other locations. This finding is consistent with the finding reported in the report *Quality and End-of-Life Care: The Right of Every Canadian, 2000* (Carstairs & Beaudoin, 2000). In this seminal document, it is reported that 75% of all deaths in Canada take place in the hospital (Carstairs & Beaudoin). Although

most people die in hospital, they may not experience quality end-of-life care, as this report also states that only 5% of dying Canadians receive integrated and interdisciplinary palliative care (Carstairs & Beaudoin). In addition, in the current health care system, there is a shortage of both nurses and hospital beds. Patients who need admission end up on stretchers in hallways of overcrowded emergency rooms when all available beds are full (Canadian Institute for Health Information, 2000). In the event a bed becomes available, the designated unit frequently does not match the service that the patient requires. Dying patients are frequently admitted to surgical or medical units rather than to a palliative care ward.

Medical and surgical units may not be an appropriate place for individuals dying of MND or other chronic diseases. For instance, dying patients may not receive a private room, as priority is given to patients requiring isolation. Pain medication and repositioning may not be a priority for nurses who are busy preparing medical patients for invasive procedures or providing preoperative and postoperative care to surgical patients. Medical and surgical nurses may not be prepared to provide end-of-life care for patients and families. They may not be equipped, as few universities or community colleges in Canada presently offer specialized palliative care training programs (Carstairs & Beaudoin). Physicians may not receive adequate training either, as medical schools lack consistency in palliative care education programs (Carstairs & Beaudoin).

Along with a lack of theory and practical skills, health care professionals may lack a positive attitude toward individuals with MND. A recent study found hospital-based health professionals felt more negative about working with MND

patients than health professionals elsewhere (Carter, McKenna, MacLeod, Hospice & Green, 1998). This finding is reflected in the experience of individuals with MND. According to Hughes et al.'s (2005) study, individuals with MND found health care professionals were distant and unapproachable. This attitude does not contribute to quality end-of-life care for individuals suffering from and dying of MND. Other system issues including insufficient staff and bed shortages resulting in admissions to inappropriate units, jeopardize quality patient care in hospital.

Adjustments need to occur in the health care system, so that individuals dying of MND can receive quality end-of-life care and experience a peaceful death. First, palliative care services need to become a priority in the health care system (Carstairs & Beaudoin, 2000). Although, some progress has been made, since the Government of Canada established the Secretariat on Palliative and End-Of-Life Care in 2001, it is under-funded (Carstairs & Beaudoin). The Harper government has recently reduced funding to the Secretariat on Palliative and End-of-Life Care (Canadian Hospice Palliative Association, 2006). Other developments include a proposed plan for a collaborative national strategy to improve palliative and end-of-life care for Canadians (Health Canada, 2005). Many anticipate this plan will increase funding for palliative and end-of-life care, although it has yet to be fully implemented (Quality End-of-Life Care Coalition of Canada, 2005). Other necessary developments include an increased number of designated palliative care beds in hospitals and nursing homes, so those individuals dying are admitted to palliative care prepared areas.

Conclusion of MND Research Findings and Implications

This thesis study established MND as a relatively rare group of diseases in Canada. The low mortality rate of MND as a proxy for the prevalence rate, reported in this thesis study may reflect a lack of awareness regarding MND among health professionals, resulting in fewer MND disease diagnoses. More likely, however, MND is a relatively uncommon cause of mortality and thus also morbidity. Individuals with MND are tending to live longer, although this may indicate the overuse of advanced technology rather than a later onset or an improved course of care while suffering from a MND. In addition, this thesis study established that more individuals with MND are married than not married. As spouses are most often the caregivers, this finding raises many concerns about caregiver burden. Women are most likely to experience caregiver burden, as they are the most common providers of informal care. A concern regarding the care for women suffering from MND is also apparent, as there has been an increase in female cases of MND over time. Increased formal support is required for women with MND, as they tend to have fewer informal caregivers available to them, despite more caregiving responsibilities.

A comprehensive home care strategy is clearly necessary, where individuals and families are not burdened by the cost of care. As well, compassionate care benefits need to be expanded significantly to include self-employed persons and individuals who work part-time. Caregivers should not be penalized for providing care through a half salary during the caregiving period. Increased funding for palliative and end-of-life care is also necessary, as all dying individuals deserve a

peaceful and pain-free death. Other important changes include increased education and training in palliative care or end-of-life care for health professionals. All health care professionals should have mandatory palliative and end-of life care education. Additional research regarding the needs of caregivers is also required, so programs and policy reflect their needs.

CHAPTER SIX

Conclusion

MND is a devastating group of diseases that lead to severe disability and premature death. Initially symptoms include twitching, cramping, and muscle weakness. As the disease progressives, immobility results from pain in joints and muscle atrophy. Individuals with MND cannot communicate with their family, as slurred and nasal speech is a common symptom, accompanied with drooling. The cough reflex eventually becomes weakened, leading to aspiration. Eventually, individuals with MND have to make difficult decisions regarding artificial life support, as invasive ventilation and a gastrointestinal tube for nutrition will be required. Although MND is considered rare, its impact has a significant effect on individuals, family, and friends. The devastating nature of MND is confounding by the knowledge that there is no cure, with only one drug Riluzole to slow its progression, and that early death will be the inevitable end.

Few Canadian research studies investigating mortality trends of MND have been completed. Only five studies have been published one to two decades ago. As such, the purpose of this thesis study was to examine mortality trends of MND in Canada to determine whether MND is becoming more or less common and to explore other trends associated with MND; such as prevalence, age, gender, birthplace, marital status, provincial trends, and location of death. A descriptive-comparative research design was used involving a mortality database from Statistics Canada. The entire population who died of MND from 1979 to 1999 was studied against all other deaths taking place in those years in Canada.

Five major findings resulted from this thesis study. First, MND is a rare cause of death in Canada. The rare nature of MND may be the result of low awareness among health professionals and inadequate diagnostic tests leading to few MND diagnoses. An increased awareness among health professionals and the general public about MND is needed to ensure those persons affected can receive accurate diagnosis and proper treatment. With increased awareness, more individuals may be diagnosed and improvements in diagnostic tools made. This thesis study also established that MND cases have increased over time. Further research, however, is required to determine whether MND is continuing to increase after 1999.

Second, the mean age at death from MND in Canada has increased over time. Since no cure for MND has been established, this increased life expectancy may be the result of improvements in health care technology, including artificial life support. All artificial life support interventions have ethical and practical implications. Prolonging life in a debilitated state may prolong suffering. The issue of allocation of health care resources is another important consideration, particularly as palliative care has long been viewed as not receiving adequate funding. Further research is required in several areas including, pharmaceutical and gene research, as this may establish a cure for MND or improve the number and type of available treatments. As the cause of MND is also not yet evident, additional epidemiological research is necessary to hopefully prevent this disease from occurring.

Third, individuals with MND are more often married that not married. This finding has many implications regarding caregiver burden, as spouses usually become caregivers for their ill partner. Informal caregivers experience physical, financial, and emotional strain as a result of caregiving. They receive little financial or other support from the government despite their significant contributions to health care. The *Compassionate Care Act,* passed in 2004, provides minimal financial support to working caregivers. Home care is also limited, with restrictions in professional and non-professional hours (Wilson et al., 2005). Home care is often limited to physical care of the ill person, and not respite or emotional support of caregivers. Family and friends absorb much of the burden and costs of home care. A comprehensive home care strategy is required that provides more professional and non-professional support to both the caregivers and the ill individuals. Significant changes to the *Compassionate Care Act* are required, including expanding the eligibility of benefits to part-time employees, stay-at-home parents, and seniors. As well, increasing the amount of compensation for caregivers is important as they only receive half their salary while caregiving. Further research investigating the needs of caregivers is necessary so that family support programs and other government policies reflect these needs. This research will also inform the ALS Society of Canada, as a low satisfaction rating for its services demonstrates a need to use evidence to improve them.

Fourth, cases of MND are increasing among females. As women are more typically informal caregivers, the care of women with MND is of some concern, particularly as research has shown male-dominated care networks provide fewer

hours of care than female-dominated care networks (Fast et al., 2003). Women have more unmet needs than men, and will therefore depend more on formal sources of care. Consequently, more women may be required to move from their home to a nursing home, hospice, or hospital to receive care. This increase in female cases of MND requires further epidemiological research and explanation as other research has not shown this trend. One such explanation may be societal changes, with more females occupying positions previously held by men. More women may be exposed to occupational toxins causing MND now than before.

Finally, more individuals with MND die in hospital that in other locations. There are many issues with hospital-based deaths. In the current strained health care system, individuals with MND may not experience a peaceful death, as there is a shortage of nurses and a shortage of palliative care beds. As mentioned, the Harper government has recently reduced funding for palliative care (Canadian Hospice Palliative Association, 2006). As a result, individuals with MND may not experience a peaceful death in hospital now, or in the coming years. Changes need to occur in the health care system that makes palliative care a priority for development. These changes include an increase in the number of hospital beds for palliative care and implementing palliative care standards of practice.

In conclusion, this thesis study of MND mortality trends in Canada for 1979–99 has revealed some key findings for practice and policy developments. While persons with MND are living longer, despite this crippling disease, ethical issues and family caregiver issues may have become more acute over time. Thankfully, MND is a relatively rare cause of death and disability in Canada.

Further research is needed, not only to improve the care and prevent MND, but also to track MND in 2000 and beyond.

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